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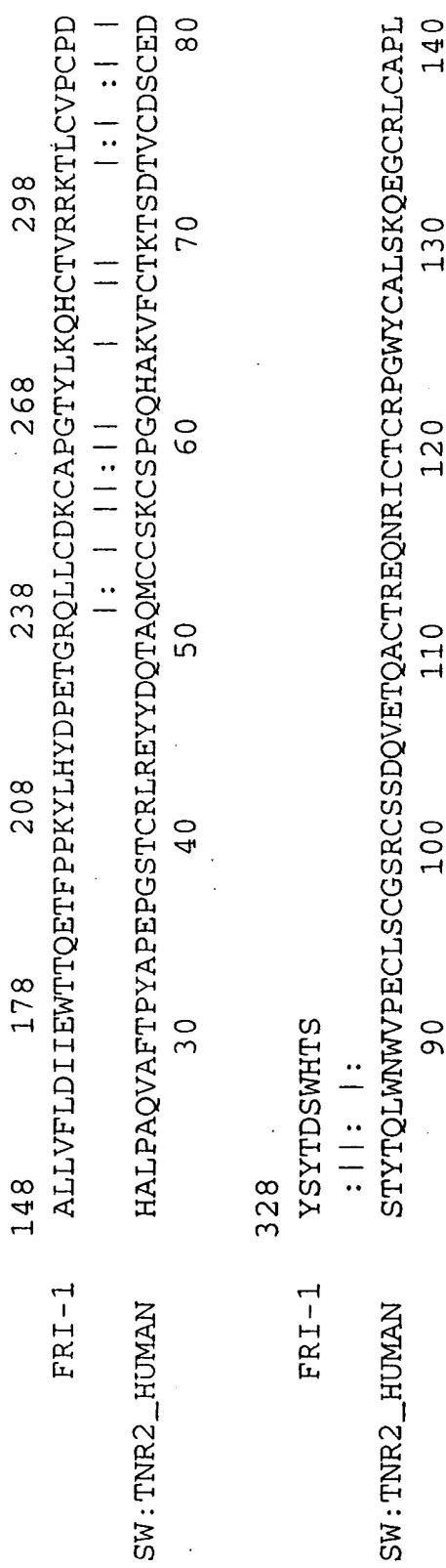
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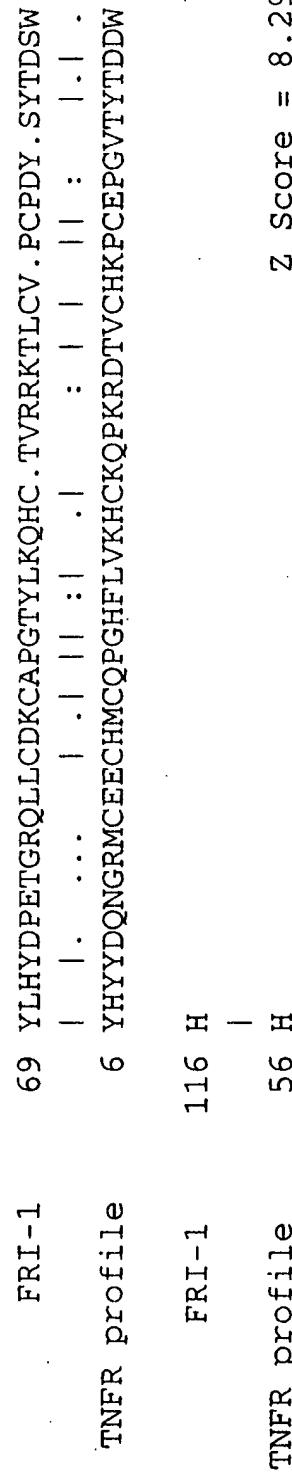
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TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 1A



## FIG. 1B



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FIG. IC

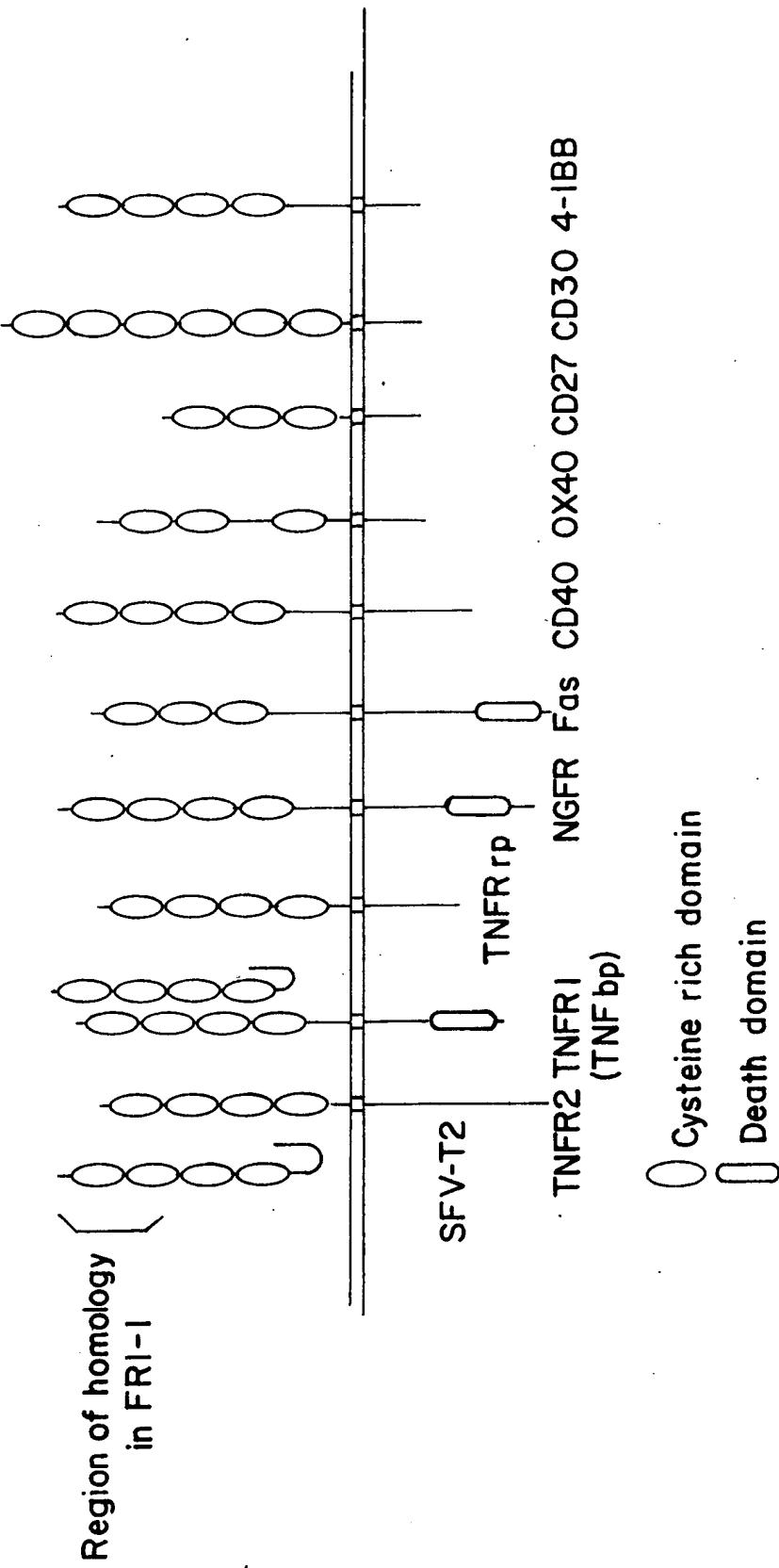


FIG. 2A

The diagram illustrates a polyA<sup>+</sup> mRNA molecule. At the 5' end, a black oval labeled "SP" represents the cap structure. A long horizontal bar represents the coding sequence, ending at a white box labeled "TAG". Above the bar, the sequence "AUG" is at the start, and "TAG" is at the stop. Three asterisks ("\*\*\*") are positioned between the AUG and TAG boxes, indicating the reading frame. The 3' end of the molecule is represented by a series of black ovals of decreasing size, representing the poly-A tail.

**FIG. 2B**

10 30 50  
 ATCAAAGGCAGGGCATACTTCCTGTTGCCAGACCTTATATAAAACGTCACTGTTGCCCTG  
 70 90 110  
 GGCAGCAGAGAACCTAGCACTGGCCAGCGGCTGCCCTGAGGTTCCAGAGGACC  
 130 150 170  
 ACAATGAACAAAGTGGCTGTGCACCTGGTGTCTGGACATCATTGAATGGACA  
M N K W L C C A L L V F L D I E W T  
 190 210 230  
 ACCCAGGAAACCTTCCTCCAAAATACTTGCAATTATGACCCAGAAACCGGACGTCAGCTC  
T O E T F P P K Y L H Y D P E T G R Q L  
 250 270 290  
 TTGTGTGACAAATGTGCTCCTGGCACCTACCTAAAACAGCACTGCACAGTCAGGAGGAAG  
 L C D K C A P G T Y L K Q H C T V R R K  
 310 330 350  
 AACACTGTGTGTCCTGCCCTGACTACTCTTATACAGACAGCTGGCACACCGAGTGATGAA  
 T L C V P C P D Y S Y T D S W H T S D E  
 370 390 410  
 TGCGTGTACTGCAGCCCCGTGCAAGGAACTGCAGACCGTGAAACAGGAGTGCAACCGC  
 C V Y C S P V C K E L Q T V K Q E C **N** R  
 430 450 470  
 ACCCACAACCGAGTGTGCAATGTGAGGAAGGGCGTACCTGGAGCTCGAATTCTGCTTG  
 T H N R V C E C E E G R Y L E L E F C L  
 490 510 530  
 AAGCACCGGAGCTGTCCCCCAGGGCTGGGTGTGCTGCAGGCTGGGACCCCCAGAGCGAAC  
 K H R S C P P G L G V L Q A G T P E R N  
 550 570 590  
 ACGGTTGCAAAAGATGTCCGGATGGTTCTCTCAGGTGAGACGTCATCGAAAGCACCC  
 T V C K R C P D G F F S G E T S S K A P  
 610 630 650  
 TGTAGGAAACACACCAACTGCAGCTCACTGGCCTCCTGCTAATTCAAGAAAGGAAATGCA  
 C R K H T **N** C S S L G L L L I Q K G **N** A  
 670 690 710  
 ACACATGACAATGTATGTCGGAAACAGAGAAGCAACTCAAAATTGTGGAATAGATGTC  
 T H D N V C S G N R E A T Q N C G I D V  
 730 750 770  
 ACCCTGTGCGAAGAGGCATTCTCAGGTTGCTGTGCCTACCAAGATTATACCGAATTGG  
 T L C E E A F F R F A V P T K I I P N W  
 790 810 830  
 CTGAGTGTCTGGTGGACAGTTGCCTGGACCAAAAGTGAATGCAGAGAGTGTAGAGAGG  
 L S V L V D S L P G T K V N A E S V E R  
 850 870 890  
 ATAAAACGGAGACACAGCTCGCAAGAGCAAACCTTCCAGCTACTTAAGCTGTGGAAGCAT  
 I K R R H S S Q E Q T F Q L L K L W K H  
 910 930 950  
 CAAAACAGAGACCAGGAAATGGTGAAGAAGATCATCCAAGACATTGACCTCTGTGAAAGC  
 Q N R D Q E M V K K I I Q D I D L C E S  
 970 990 1010  
 AGTGTGCAACGGCATATCGGCCACCGAACCTCACCAAGAGCAGCTCCGCATCTGATG  
 S V Q R H I G H A N L T T E Q L R I L M

FIG. 2C

1030	1050	1070
GAGAGCTTGCCTGGGAAGAAGATCAGCCCAGACGAGATTGAGAGAACGAGAAAGACCTGC		
E S L P G K K I S P D E I E R T R K T C		
1090	1110	1130
AAACCCAGCGAGCAGCTCCTGAAGCTACTGAGCTTGTGGAGGATCAAAATGGAGACCAA		
K P S E Q L L K L L S L W R I K N G D Q		
1150	1170	1190
GACACCTTGAAGGGCCTGATGTACGCACTCAAGCACTTGAAAGCATACCACTTCCAAA		
D T L K G L M Y A L K H L K A Y H F P K		
1210	1230	1250
ACCGTCACCCACAGTCTGAGGAAGACCACAGGTTCTTGCACAGCTCACCATGTACCGA		
T V T H S L R K T I R F L H S F T M Y R		
1270	1290	1310
TTGTATCAGAAACTCTTCTAGAAATGATAGGGAAATCAGGTTCAATCAGTGAAGATAAGC		
L Y Q K L F L E M I G N Q V Q S V K I S		
1330	1350	1370
TGCTTATAGTTAGGAATGGTCACTGGCTTTCTTCAGGATGGGCCAACACTGATGGAG		
C L		
1390	1410	1430
CAGATGGCTGTTCTCCGGCTTGAAATGGCAGTTGATTCTTCATCAGTTGGTGG		
1450	1470	1490
GAATGAAGATCCTCCAGCCAACACACACACTGGGAGTCTGAGTCAGGAGAGTGAGGCA		
1510	1530	1550
GGCTATTTGATAATTGTGCAAAGCTGCCAGGTGTACACCTAGAAAGTCAAGCACCCCTGAG		
1570	1590	1610
AAAGAGGATATTTTATAACCTCAAACATAGGCCCTTCCTCCTCCTATGGATGAG		
1630	1650	1670
TAATCAGAAGGCTTCTACTATCTTCTGTGTACATCCCTAGATGAAGGCCTCTTTATTTAT		
1690	1710	1730
TTTTTTATTCTTTTCGGAGCTGGGACCGAACCCAGGGCCTGCGCTTGCAGGCAA		
1750	1770	1790
GTGCTCTACCACTGAGCTAAATCTCCAACCCCTGAAGGCCTTTCTGCCTCTGAT		
1810	1830	1850
AGTCTATGACATTCTTTCTACAATTCTGATCAGGTGCACGAGCCTTATCCCATTGT		
1870	1890	1910
AGGTTCTAGGCAAGTTGACCGTTAGCTATTTCCCTCTGAAGATTGATTGAGTTGC		
1930	1950	1970
AGACTTGGCTAGACAAGCAGGGTAGTTATGGTAGTTATTAACAGACTGCCACCAGG		
1990	2010	2030
AGTCCAGTGTCTTCTGTAGTTGACTTAAGCTGACTCCAAGTACATTAGTA		
2050	2070	2090
TGAAAAATAATCAACAAATTATTCCCTCTATCAACATTGGCTAGCTTGTTCAGGGC		
2110	2130	2150
ACTAAAAGAAACTACTATATGGAGAAAGAATTGATATTCCCCAACGTTCAACAAACCA		
2170	2190	2210
ATAGTTTATCCAGCTGTACGCCCTGGTTAGTGTACTGACTATGCGCCCTCTTATTAC		
2230	2250	2270
TGCATGCAGTAATTCAACTGGAAATAGTAATAATAATAAGAAATAAAATCTAGACTCC		
2290	2310	2330
ATTGGATCTCTGAATATGGGAATATCTAACCTAACAGCTTGTGAGATTCTAGTTGTGT		
2350	2370	2390
TAAAGGCTTTATTAAAAAGCTGATGCTCTGTAAAAGTTACTAACATATCTGTAAGA		
2410	2430	
CTATTACAGTATTGCTATTATCCATCCAG		

IV.E. COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

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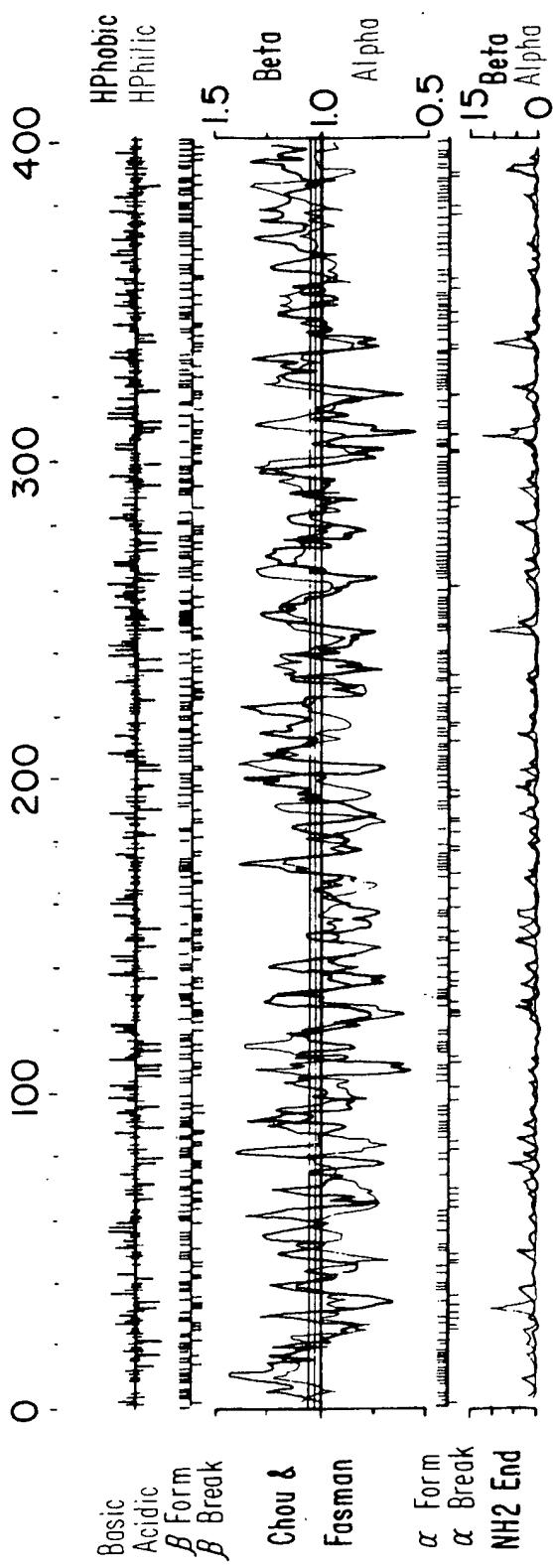
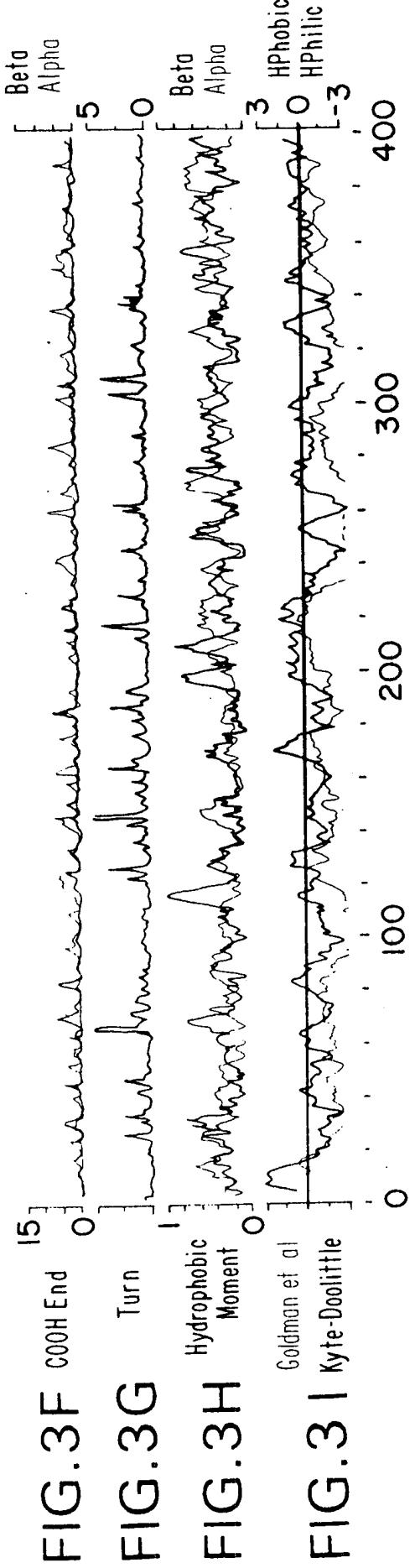


FIG. 3A  
FIG. 3B

FIG. 3C  
FIG. 3D  
FIG. 3E

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FIG.4A

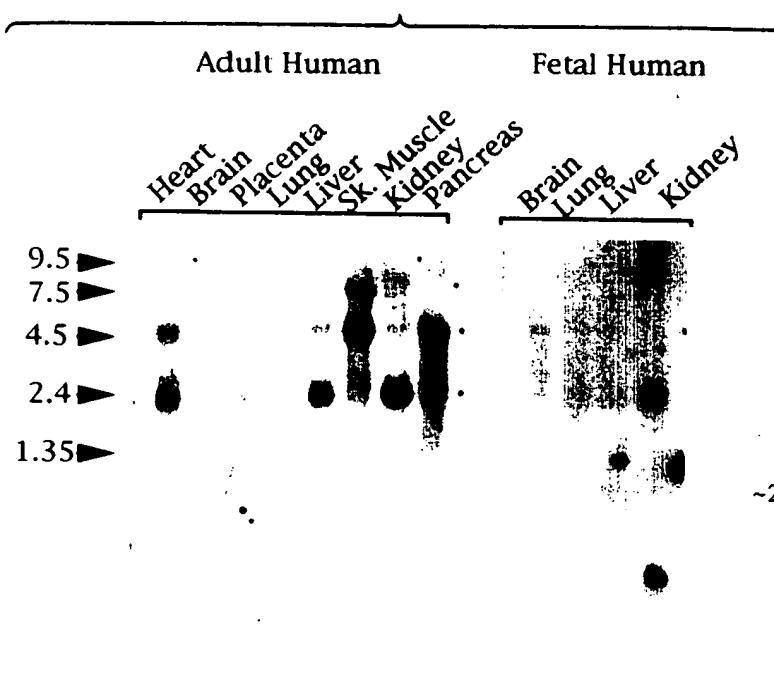
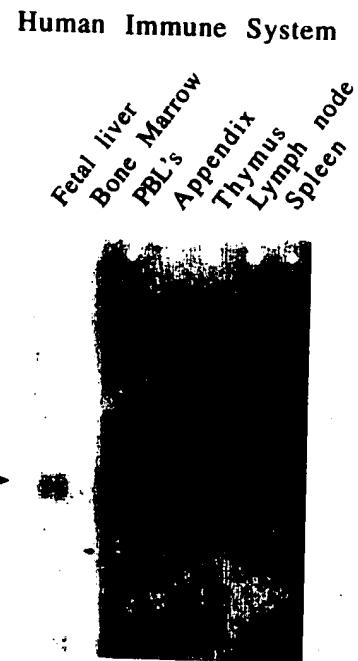
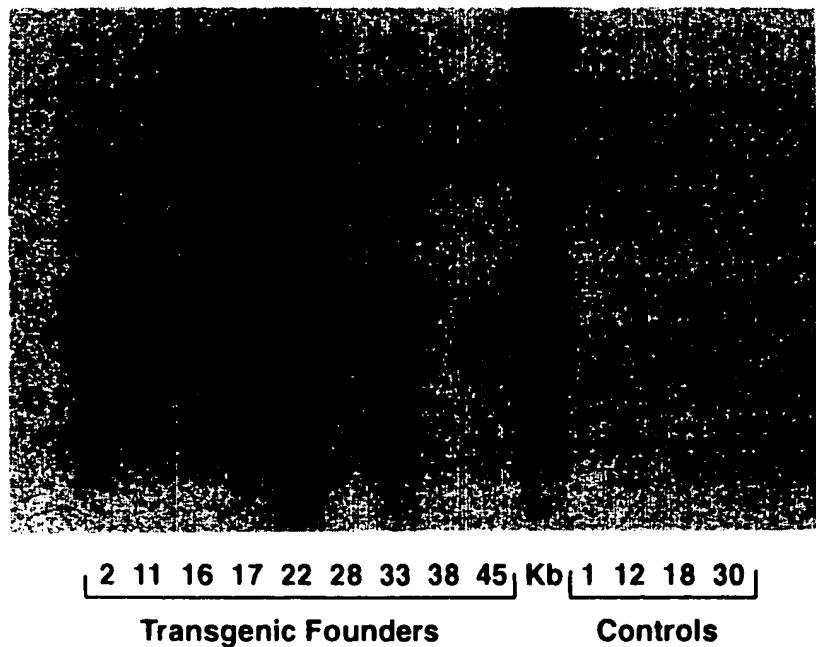


FIG.4B



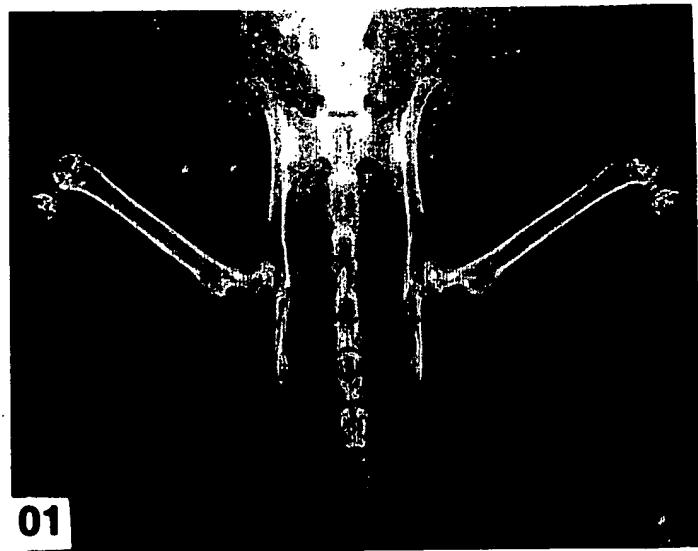
TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

# FIG. 5

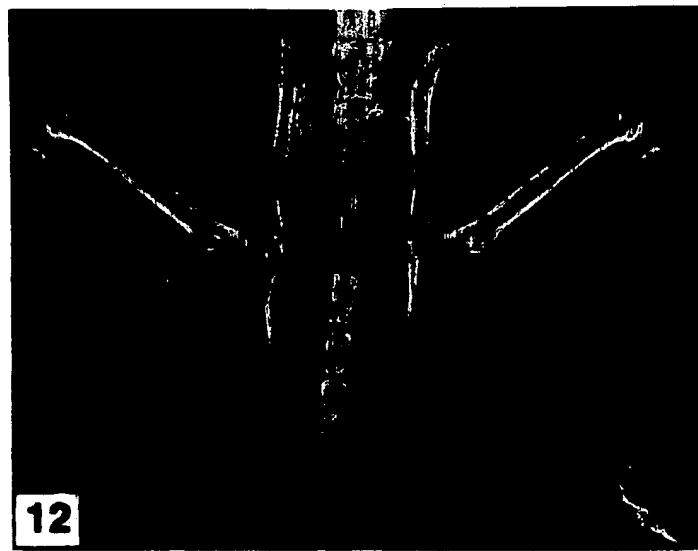


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LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

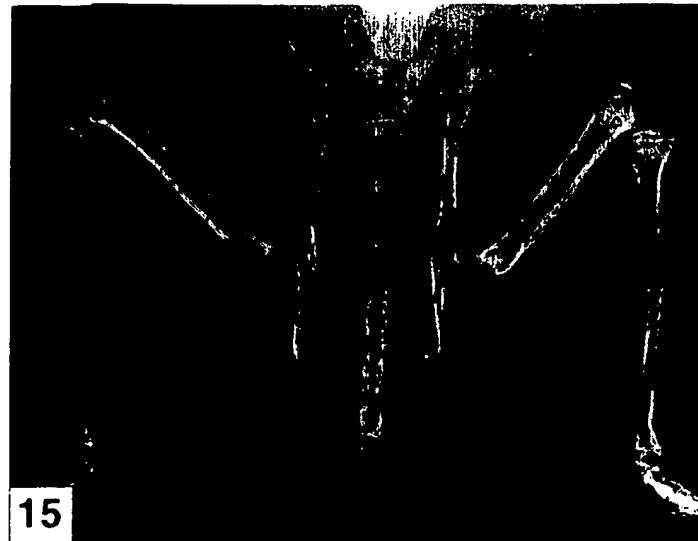
**FIG.6A**



**FIG.6B**

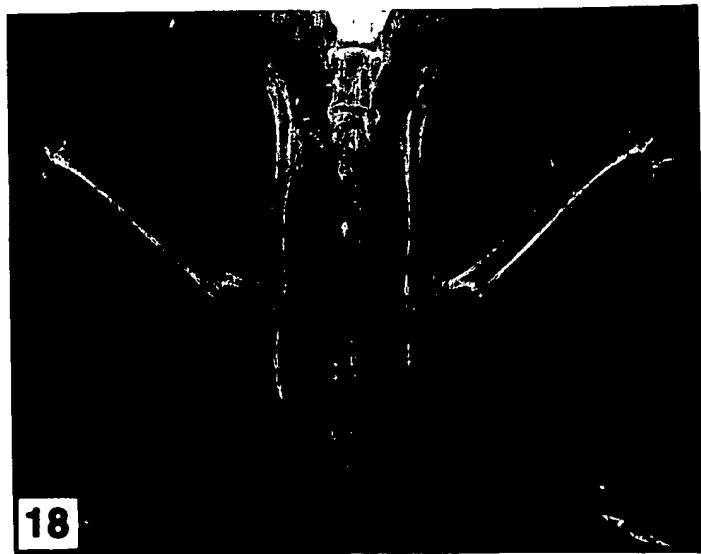


**FIG.6C**

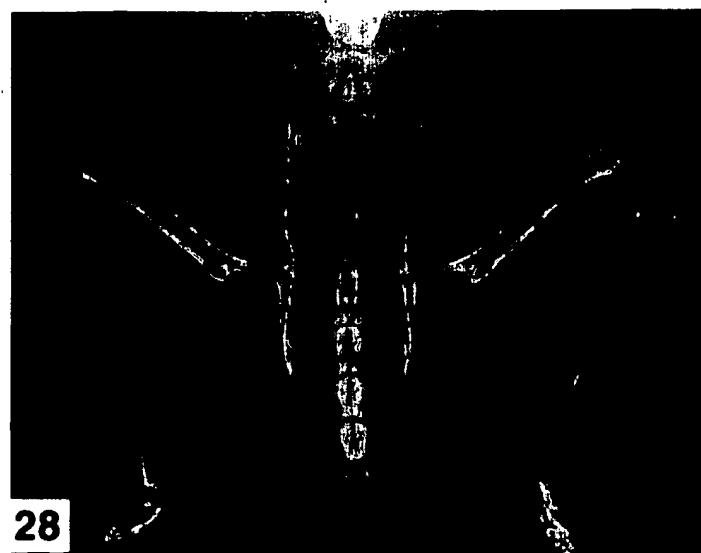


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INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

**FIG.6D**



**FIG.6E**

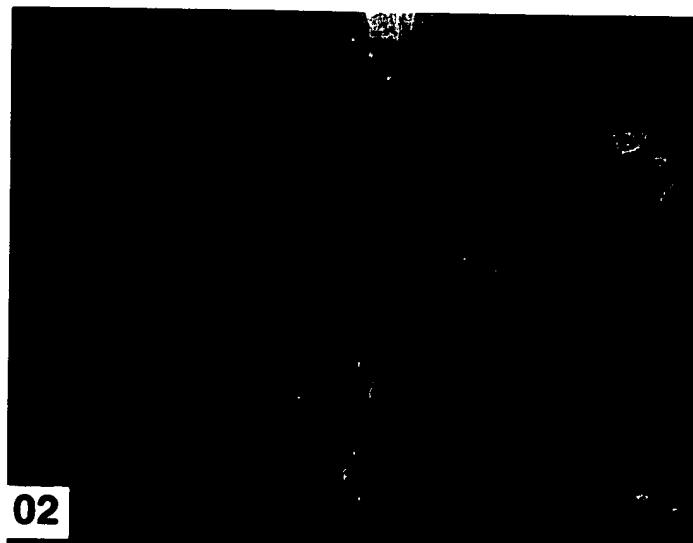


**FIG.6F**

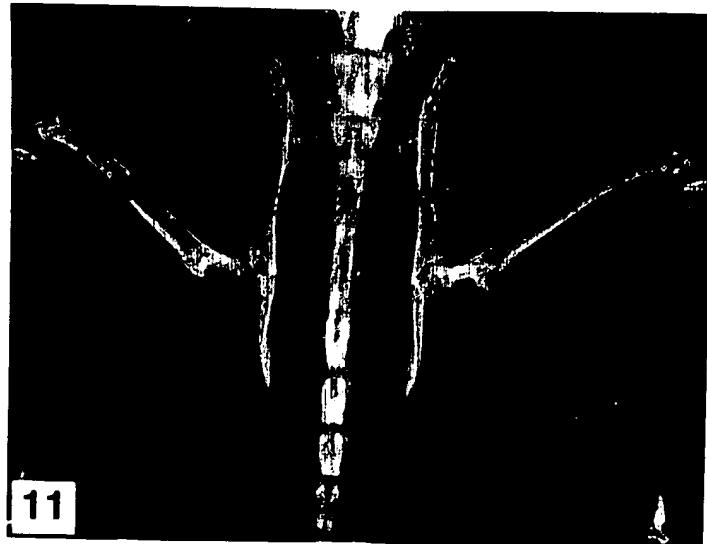


TITLE: COMBINATION THERAPY FOR CONDITIONS  
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INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

**FIG.6G**



**FIG.6H**

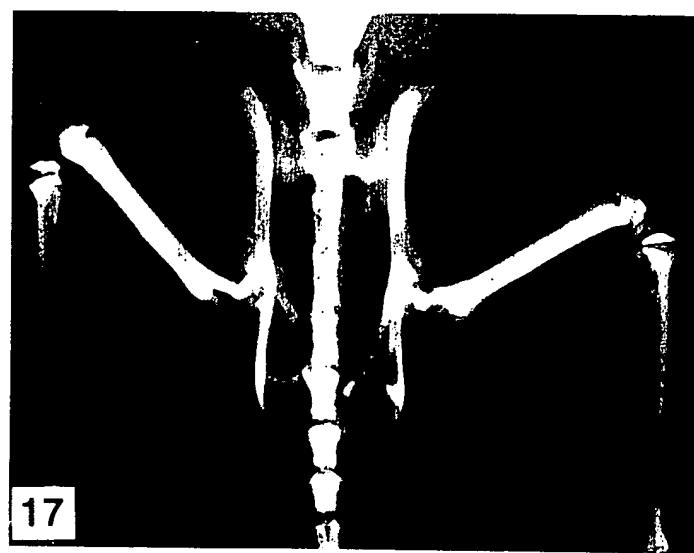


TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.6I

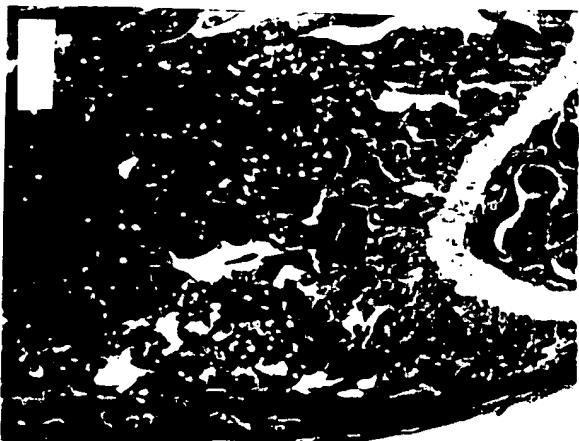


FIG.6J



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

**FIG.7A**



**FIG.7B**



**FIG.7C**



**FIG.7D**



TITLE: COMBINATION THERAPY FOR CONDITIONS  
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INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.7E



FIG.7F



FIG.7G



FIG.7H



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIPS

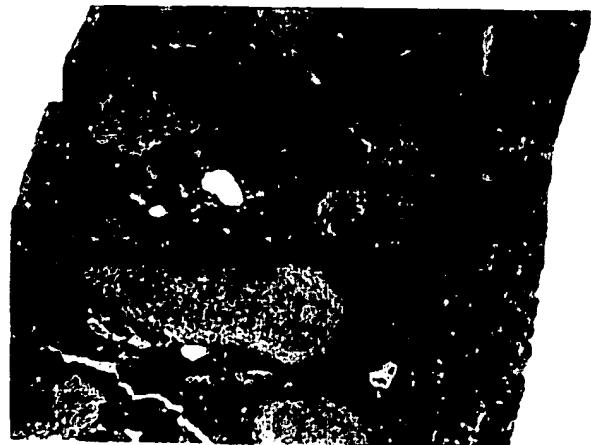
**FIG.8A**



**FIG.8B**



**FIG.8C**



**FIG.8D**



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 9A

10                   30                   50  
CCTTATATAAACGTCA TGATTGCCTGGGCTGCAGAGACGCACCTAGCACTGACCCAGCG  
70                   90                   110  
GCTGCCTCCTGAGGTTCCCAGGGACCACAATGAACAAAGTGGCTGTGCTGCGCACTCCTG  
M N K W L C C A L L  
130                   150                   170  
GTGCTCCTGGACATCAT TGAATGGACAACCCAGGAAACCCCTTCCCAAAGTACTTGCAT  
V L L D I I E W T T O E T L P P K Y L H  
190                   210                   230  
TATGACCCAGAAACTGGTCATCAGCTCCCTGTGTGACAAATG'TGCTCCTGGCACCTACCTA  
Y D P E T G H Q L L C D K C A P G T Y L  
250                   270                   290  
AAACAGCACTGCACAGTGAGGAGGAAGACATTGTGTGTCCCTGCCCTGACCAACTTTAT  
K Q H C T V R R K T L C V P C P D H S Y  
310                   330                   350  
ACGGACAGCTGGCACACCAGTGATGAGTGTGTATTGCAGCCCAGTGTGCAAGGAACCTG  
T D S W H T S D E C V Y C S P V C K E L  
370                   390                   410  
CAGTCGGTAAGCAGGAGTGCAACCGCACCCACAACCGAGTGTGTGAGTGTGAGGAAGGG  
Q S V K Q E C M R T H N R V C E C E E G  
430                   450                   470  
CGTTACCTGGAGATCGAATTCTGCTTGAAGCACCGAGCTGTCCCCGGCTCCGGCGTG  
R Y L E I E F C L K H R S C P P G S G V  
490                   510                   530  
GTGCAAGCTGGAACCCCAGAGCGAAACACAGTTGCAAAAATGTCCAGATGGGTTCTTC  
V Q A G T P E R N T V C K K C P D G F F  
550                   570                   590  
TCAGGTGAGACTTCATCGAAAGCACCCCTGTATAAAACACACGAACTGCAGCACATTGGC  
S G E T S S K A P C I K H T N C S T F G  
610                   630                   650  
CTCCTGCTAATTCAAGAAAGGAAATGCAACACATGACAACAGTGTTCCGGAAACAGAGAA  
L L L I Q K G M A T H D N V C S G N R E  
670                   690                   710  
GCCACGCAAAAGTGTGGAATAGATGTCACCCGTGTGAAGAGGCCTTCAGGTTGCT  
A T Q K C G I D V T L C E E A F F R F A  
730                   750                   770  
GTTCCCTACCAAGATTATACCAAATTGGCTGAGTGTGTTGGACAGTTGCCTGGGACC  
V P T K I I P N W L S V L V D S L P G T

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## FIG.9B

790 810 830  
AAAGTGAATGCCGAGACTGTAGAGAGGATAAAACGGAGACACAGCTCACAAAGAGCAAACC  
K V N A E S V E R I K R R H S S Q E Q T  
850 870 890  
TTCCAGCTGCTGAAGCTGTGGAAACATCAAAACAGAGAGCAGGAAATGGTGAAGAAGATC  
F Q L L K L W K H Q N R D Q E M V K K I  
910 930 950  
ATCCAAGACATTGACCTCTGTGAAAGCAGCGTGCAGCGGCATCTCGGCCACTCGAACCTC  
I Q D I D L C E S S V Q R H L G H S N L  
970 990 1010  
ACCACAGAGCAGCTTCTTGCTTGATGGAGAGCCTGCCTGGAAAGAAGATCAGCCCAGAA  
T T E Q L L A L M E S L P G K K I S P E  
1030 1050 1070  
GAGATTGAGAGAACGAGAAAGACCTGCAAATCGAGCGAGCAGCTCCTGAAGCTACTCACT  
E I E R T R K T C K S S E Q L L K L L S  
1090 1110 1130  
TTATGGAGGATCAAAAATGGTGACCAAGACACCTTGAAGGGCCTGATGTATGCCCTCAAG  
L W R I K N G D Q D T L K G L M Y A L K  
1150 1170 1190  
CACTTGAAACATCCCACCTTTCACCAAAACTGTCACCCACAGTCTGAGGAAGACCATGAGG  
H L K T S H F P K T V T H S L R K T M R  
1210 1230 1250  
TTCCTGCACAGCTTCACAATGTACAGACTGTATCAGAAGCTTTAGAAATGATAGGG  
F L H S F T M Y R L Y Q K L F L E M I G  
1270 1290 1310  
AATCAGGTTCAATCCGTAAAATAAGCTGCTTATAACTAGGAATGGTCACTGGGCTGTTT  
N Q V Q S V K I S C L  
  
CTTCA

**TITLE: COMBINATION THERAPY FOR CONDITIONS  
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**INVENTORS: Boyle, et al.**

**APPLN. NO: A-378CIP5**

FIG.9C

TITLE: COMBINATION THERAPY FOR CONDITIONS  
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APPLN. NO: A-378CIP5

## FIG.9D

790 810 830  
CACCAAAGTAAACGCAGAGAGTGTAGAGAGGATAAAACGGCAACACAGCTCACAAGAAC  
T K V N A E S V E R I K R Q H S S S Q E Q  
850 870 890  
GACTTTCCAGCTGCTGAAGTTATGGAAACATCAAAACAAAGACCAAGATATAGTCAAGAA  
T F Q L L K L W K H Q N K D Q D I V K K  
910 930 950  
GATCATCCAAGATATTGACCTCTGTGAAAACAGCGTGCAGCGGCACATTGGACATGCTAA  
I I Q D I D L C E N S V Q R H I G H A N  
970 990 1010  
CCTCACCTTCGAGCAGCTTCGTAGCTTGATGGAAAGCTTACCGGGAAAGAAAGTGGGAGC  
L T F E Q L R S L M E S L P G K K V G A  
1030 1050 1070  
AGAAGACATTGAAAAAACATAAAGGCATGCAAACCCAGTGACCAGATCCTGAAGCTGCT  
E D I E K T I K A C K P S D Q I L K L L  
1090 1110 1130  
CAGTTTGTGGCGAATAAAAATGGCGACCAAGACACCTTGAAGGGCTAATGCACGCACT  
S L W R I K N G D Q D T L K G L M H A L  
1150 1170 1190  
AAAGCACTCAAAGACGTACCACTTTCCAAAACTGTCACTCAGAGTCTAAAGAAGACCAT  
K H S K T Y H F P K T V T Q S L K K T I  
1210 1230 1250  
CAGGTTCTTCACAGCTTCACAATGTACAAATTGTATCAGAAGTTATTTTAGAAATGAT  
R F L H S F T M Y K L Y Q K L F L E M I  
1270 1290 1310  
AGGTAACCAGGTCCAATCAGTAAAATAAGCTGCTTATAACTGAAATGGCCATTGAGCT  
G N Q V Q S V K I S C L  
1330 1350  
GTTTCCTCACAAATTGGCGAGATCCCATGGATGATAA

FIG. 9E

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APPLN. NO: A-378CIP5

50  
50  
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100  
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100

150  
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850  
850  
850  
850

900  
900  
900  
900

# FIG. 9F

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osteо.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S L P G T K V N A E S V E R I K R H A S S Q E Q T	250
osteо.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S I P G T K V N A E S V E R I K R H S S Q E Q T	250
osteо.frg	L C E E A F F R F A V P T K F T P N W L S V L V D N L P G T K V N A E S V E R I K R Q H S S Q E Q T	250

osteо.frg	F Q L L K L W K H Q N R D Q E M V K I I Q D I D L C E S S V Q R H L G H S N I L T E Q U L A L M E	300
osteо.frg	F Q L L K L W K H Q N R D Q E M V K I I Q D I D L C E S S V Q R H I G H A N L T E Q U R I S L M E	300
osteо.frg	F Q L L K L W K H Q N K D Q D I V K K I I Q D I D L C E N S V Q R H I G H A N L T F E Q U R S L M E	300

osteо.frg	S L P G K K I S P E E I E R T R K T C K S S E Q L L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteо.frg	S L P G K K I S P D E I E R T R K T C K P S E Q L L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteо.frg	S L P G K K V G A E D I E R T I K A C K P S D Q F I K L L S L W R I K N G D Q D T L K G L M Y A L K	350

osteо.frg	H L K T S H F P K T V T H S I R K T M R F I H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteо.frg	H L K A Y H F P K T V T H S I R K T I R F I H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteо.frg	H S K T Y H F P K T V T Q S L R K T I R F I H S F T M Y K L Y Q K L F L E M I G N Q V Q S V K I S C	400

osteо.frg	I	401
osteо.frg	I	401
osteо.frg	I	401

# FIG. 10

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

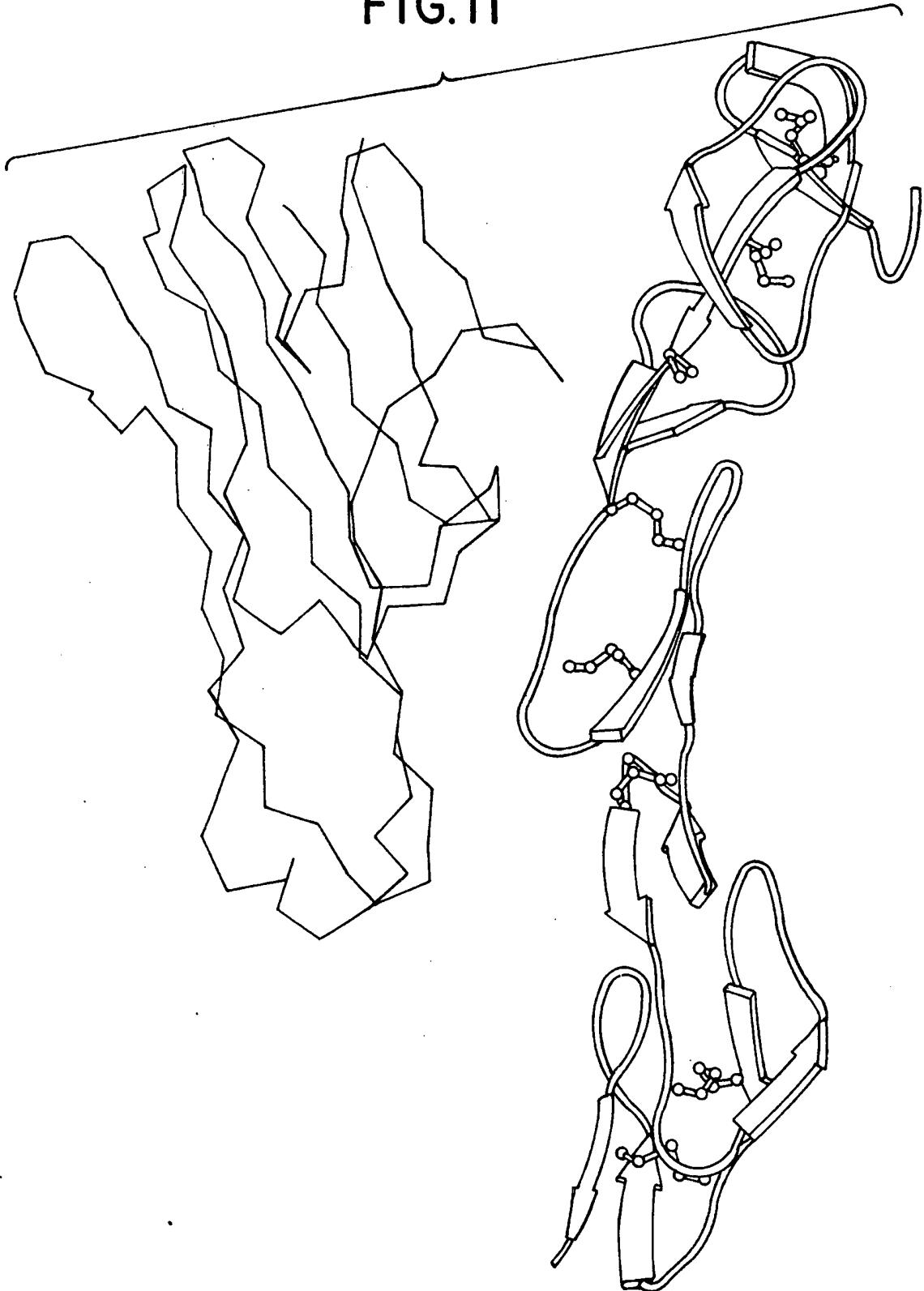
1tnrr C P Q - G K Y I H P Q N N S I C C T K C H K G T Y L Y N D C P G P G Q D T D C R E C E S G S F T A S 49  
noste P P K Y L H Y D E E T S H Q L L C D K C P P G T Y L K Q H C T A K - W K T V C A P C P D H Y Y T D S 49

1tnrr E N H L R H C L S C S - K C R K E M G O V E I S S C T V D R D T V C G C R K N Q Y R H Y W S E N L F 98  
noste W H T S D E C L Y C S P V C - K E L Q Y V K - Q E C N R T H N R V C E C K E G R Y L E I - - - E - F 93

1tnrr Q C F N C S L C L N G - T V H L S C Q E K Q N T V C T - C H A G F F L R E - - - N E C V S C 139  
noste - C L K H R S C P P G F G V V Q A G T P E R N T V C K R C P D G F F S N E T S S K A P C R K H 139

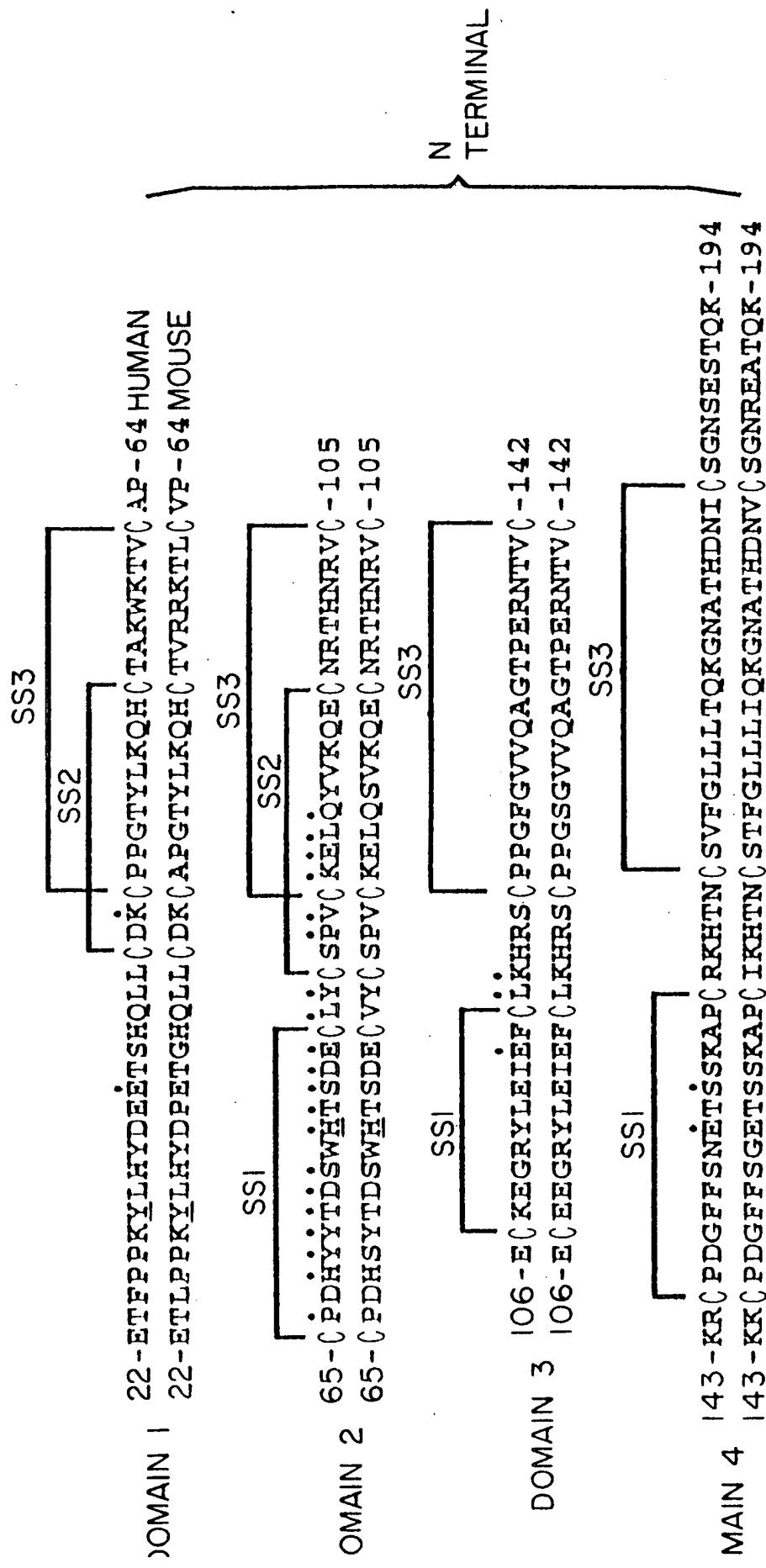
TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. II



# FIG. 12A

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIPS

FIG. 12B

195 -CGIDVTI[CEEAFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERIKRQHSS-246  
195 -CGIDVTI[CEEAFRFAVPTKIIIPNWLSQLVDSLPGTKVNAESVERIKRQHSS-246

247 -QEQTFOQLKLWKKHQNKDQDIVKKIIQDIDI[ENSVQRHIGHANLTPEQLRSI-298  
247 -QEQTFOQLKLWKKHQNRDQEMVKKIIQDIDI[CESSVQRHLGHSNLTLTEQLLAL-298

299 -MESLPGKRVGAEDIEKTIKACKPSDQIQLKLSSLWRIKNGDQDTLKGLMHALK-350  
299 -MESLPGKRVISPEIERTRKTC[KSSEQQLKLSSLWRIKNGDQDTLKGLMYALK-350

351 -HSKTYHFPKTVTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVRKISCL-401  
351 -HLKTSHFPKTVTHSLRKTMRFILHSFTMYRLYQKLFLEMIGNQVQSVRKISCL-401

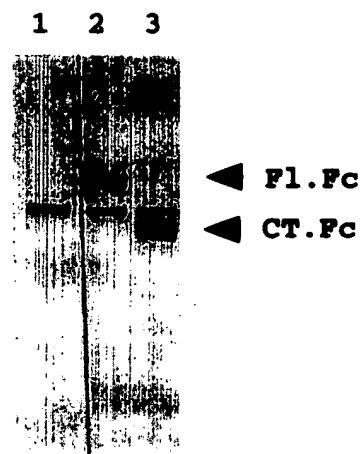
C TERMINAL

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

**FIG. 13A**



**FIG. 13B**



**FIG. 13C**

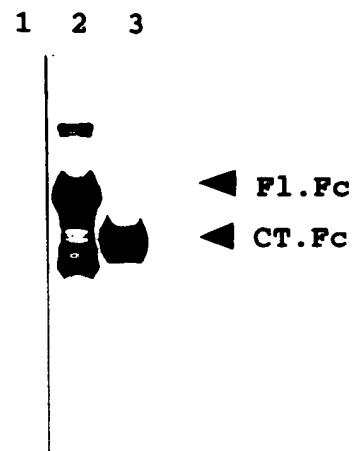
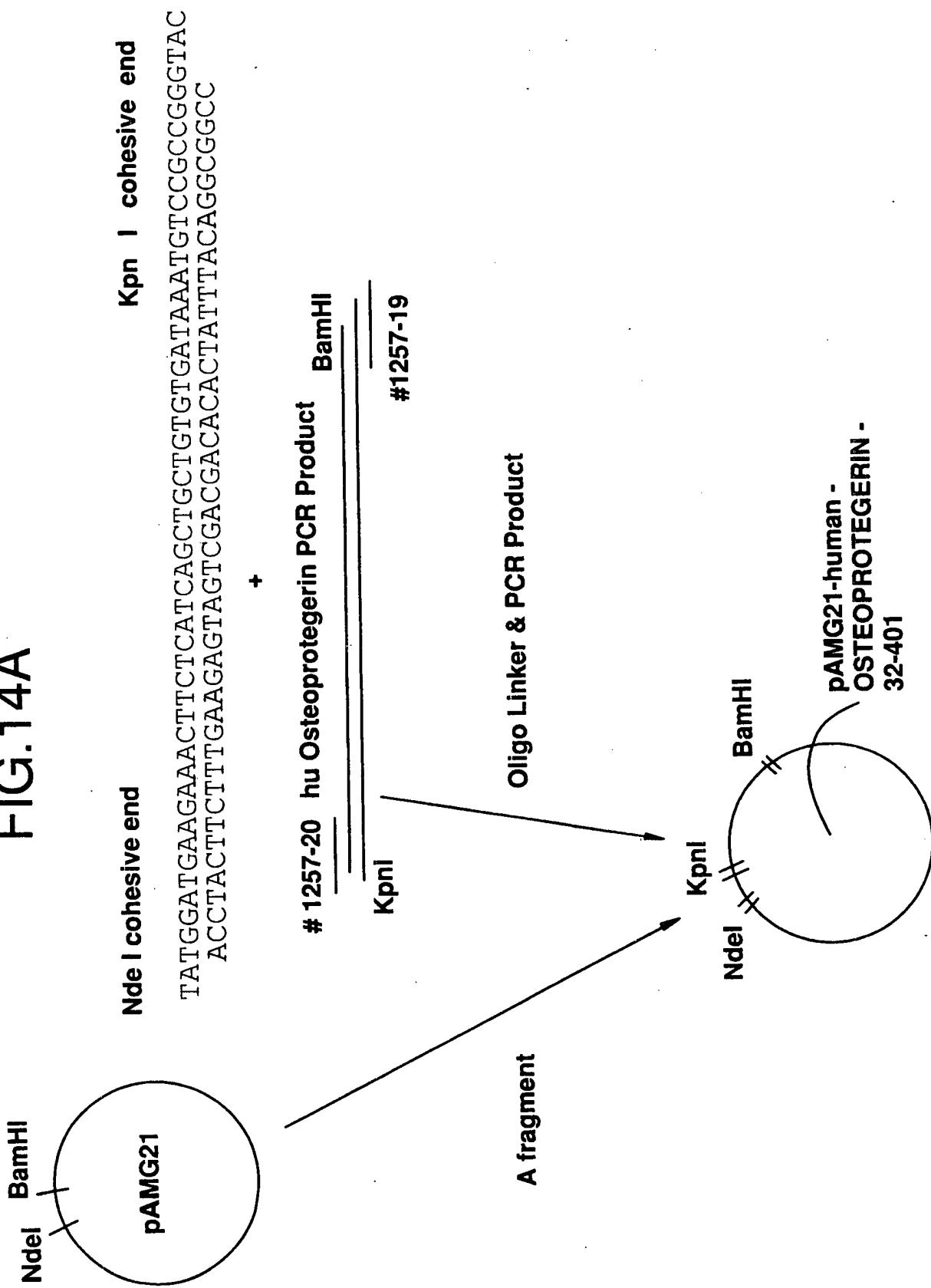
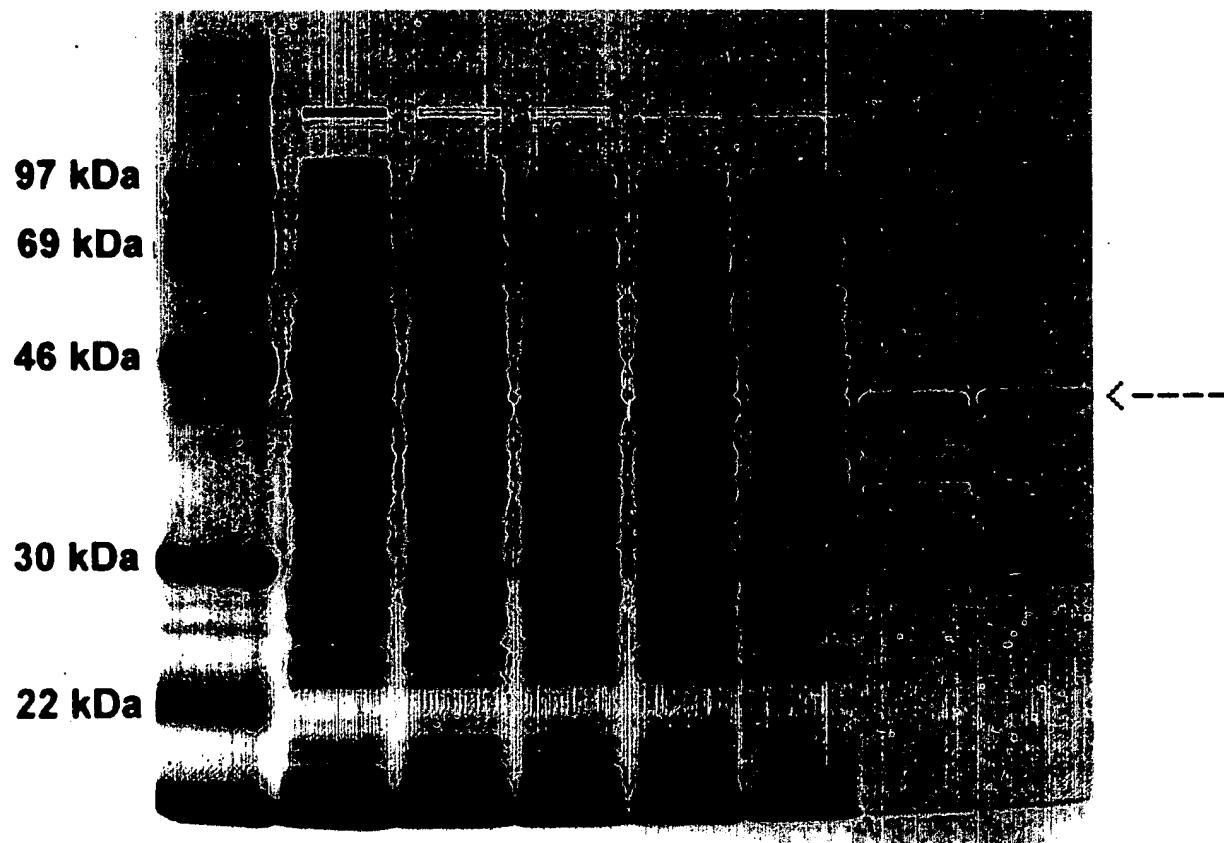


FIG. 14A



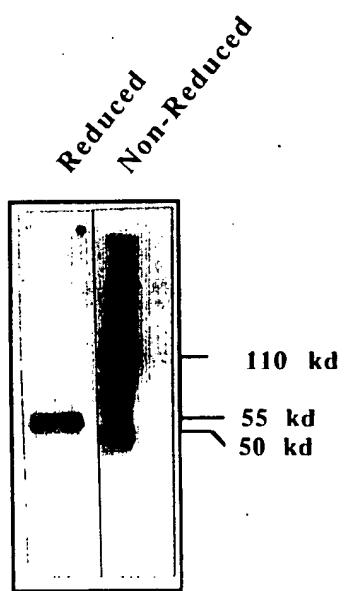
**FIG. 14B**

**Lane# 1 2 3 4 5 6 7 8**



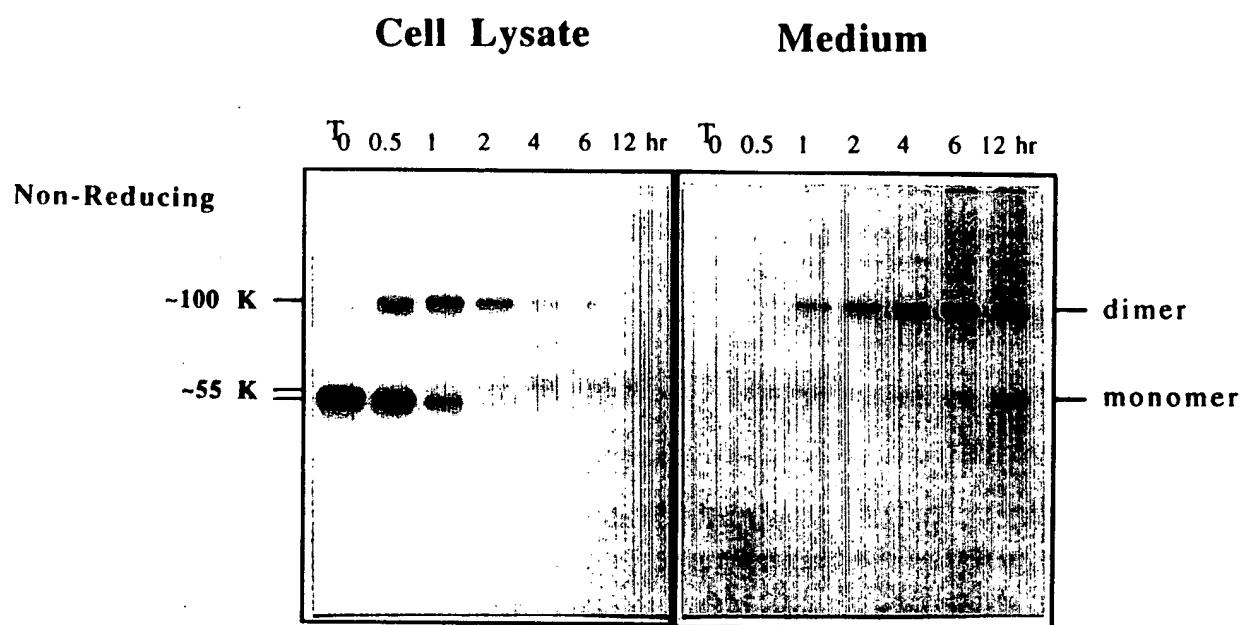
TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 15

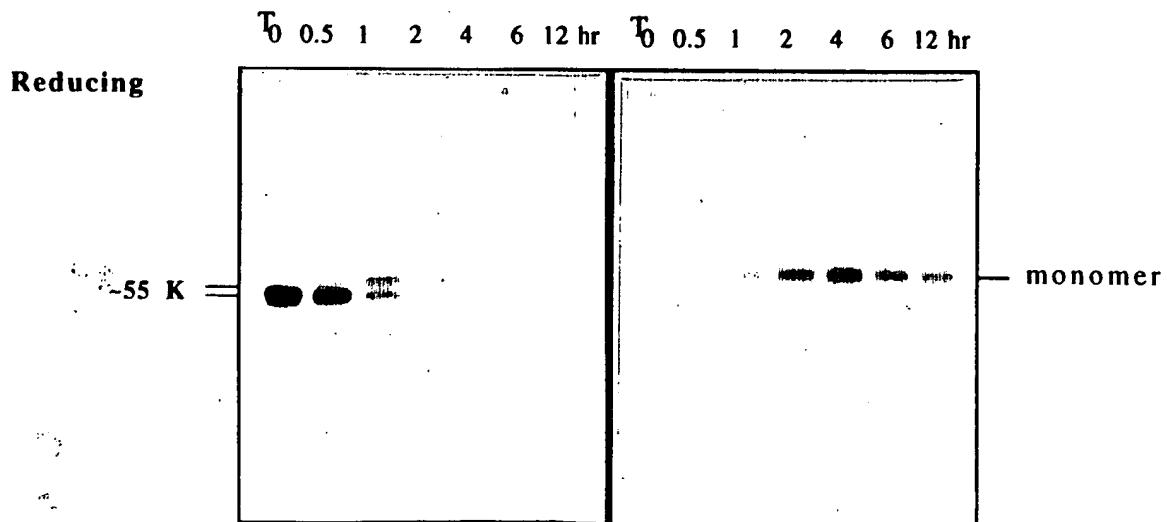


TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

**FIG.16A**

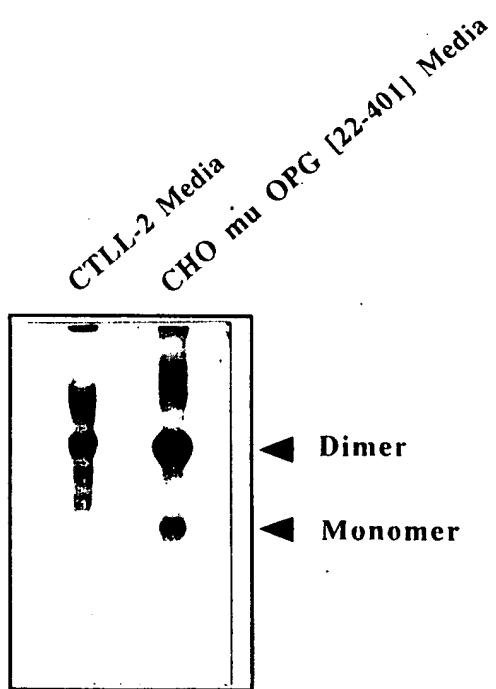


**FIG.16B**



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 17



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIPS

FIG. 18

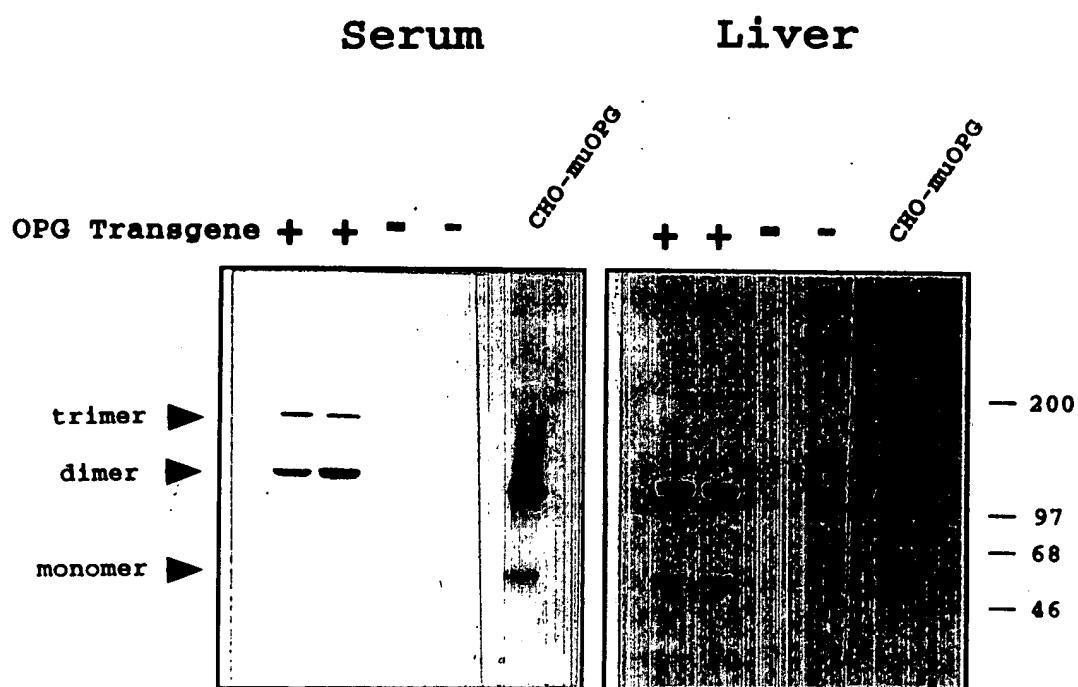


FIG. 19A

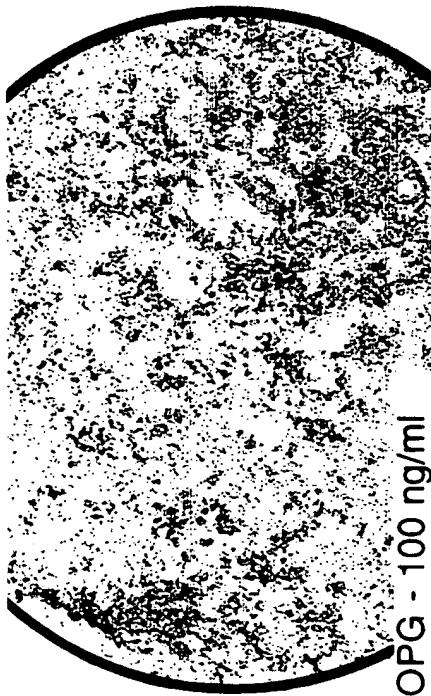


FIG. 19C



FIG. 19B

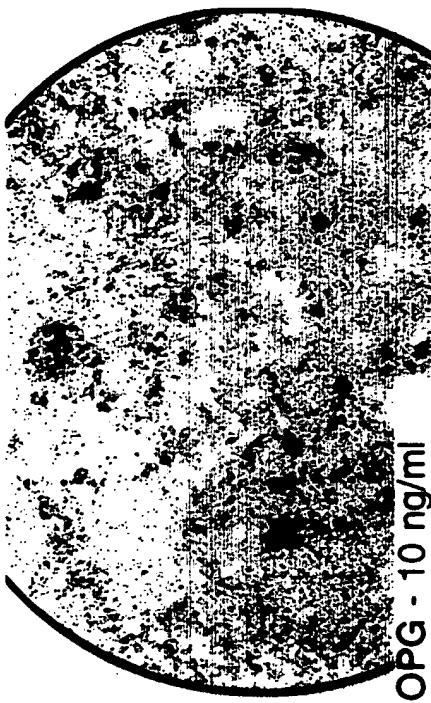
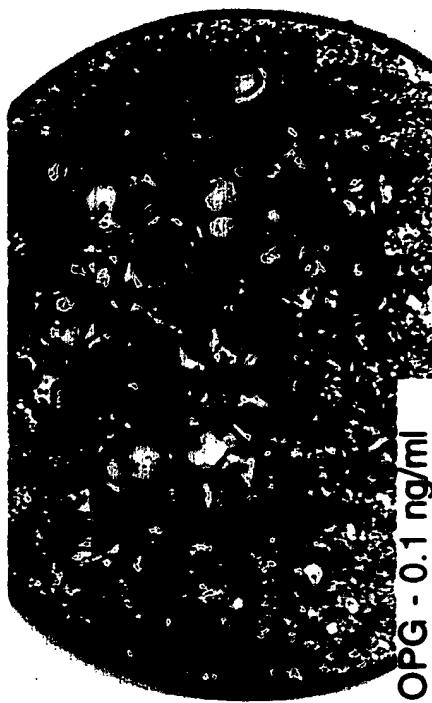
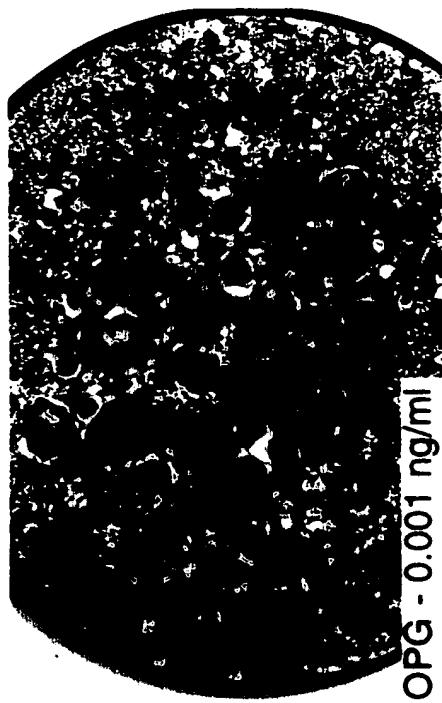


FIG. 19D



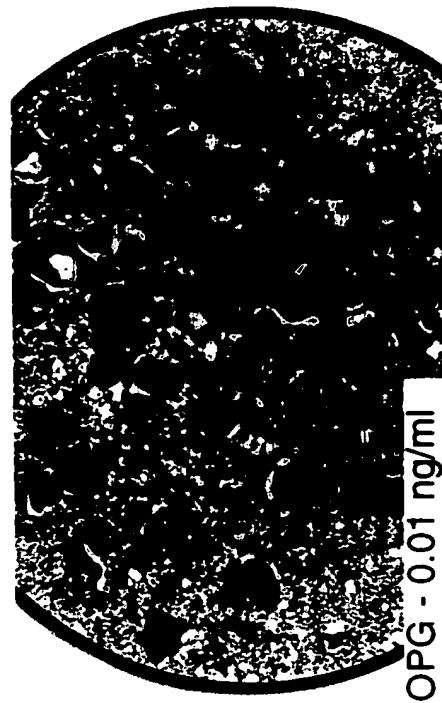
TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. 19F



OPG - 0.001 ng/ml

FIG. 19E



OPG - 0.01 ng/ml

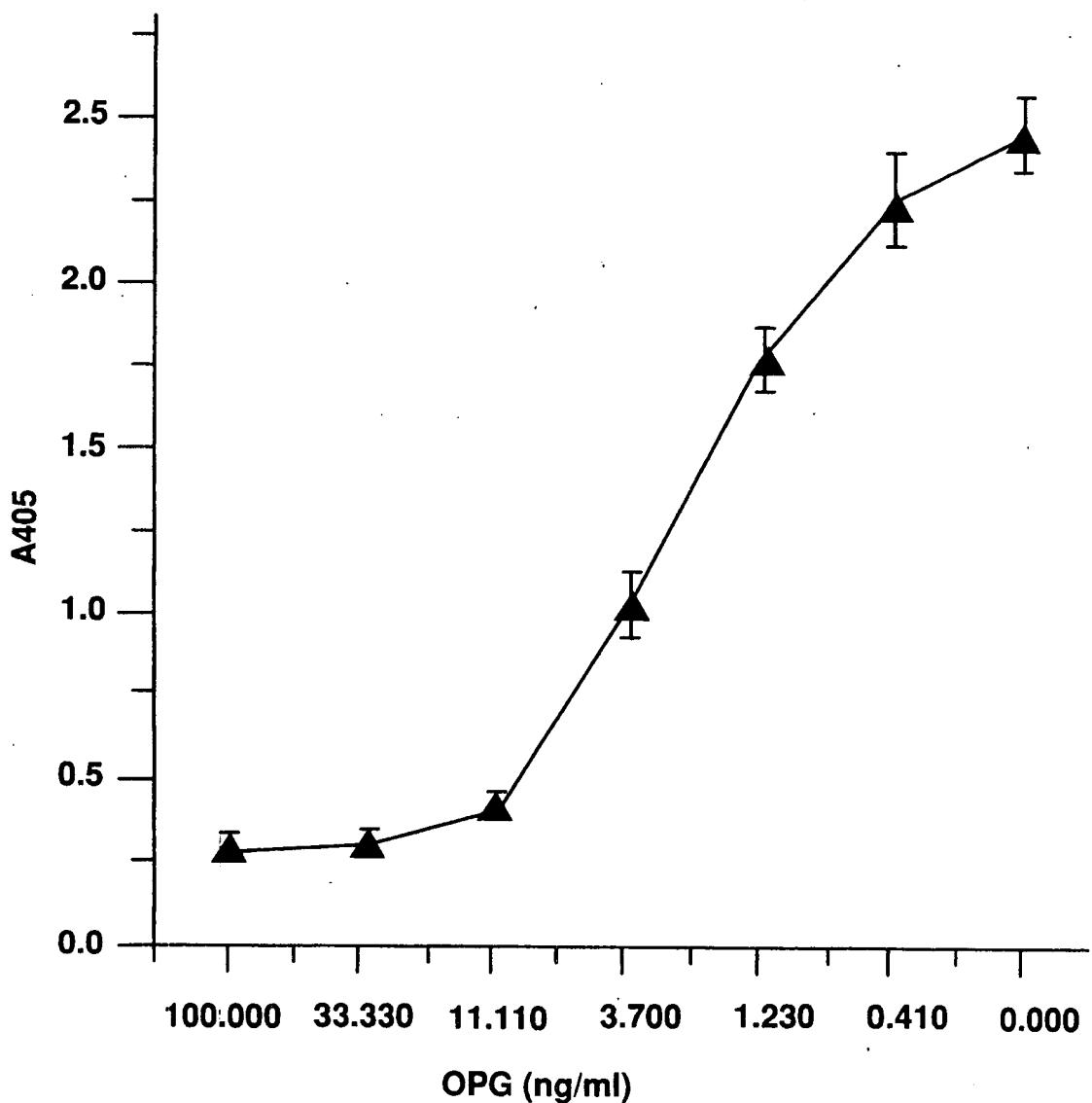
FIG. 19G



Control

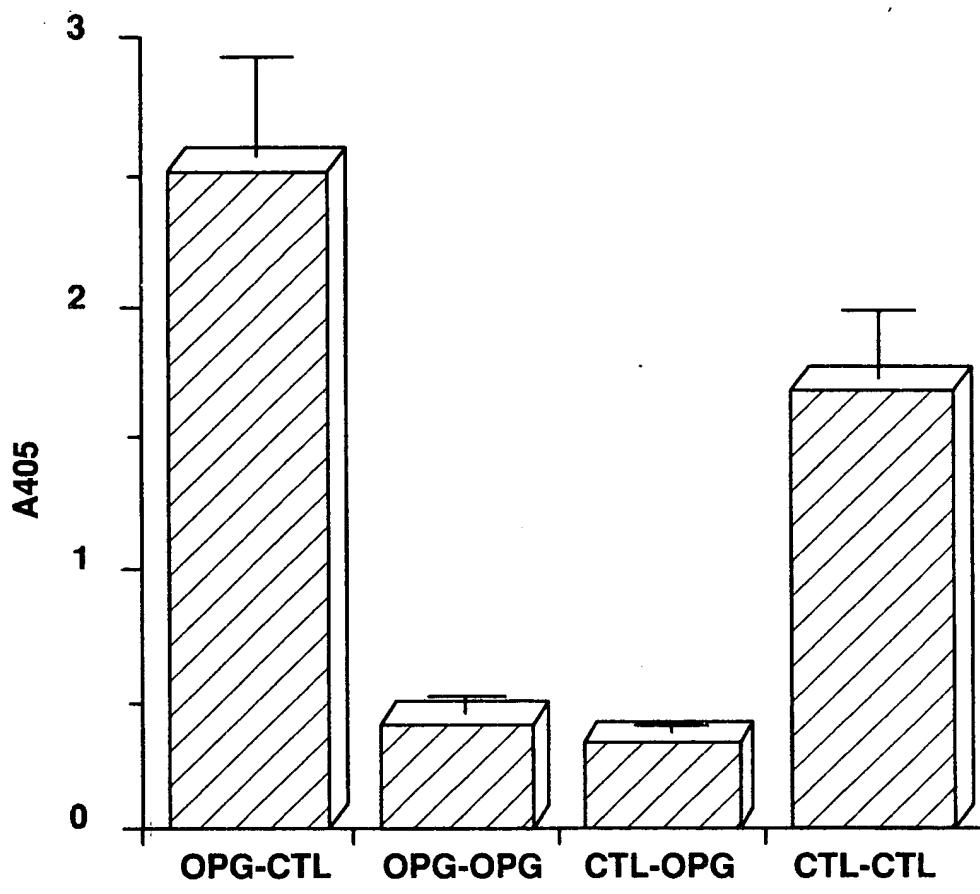
TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.20



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.21



Legend

Growth Bone marrow cells CSF -1	Intermediate PGE2 + CSF-1	Terminal ST2 cells 1,25 (OH) <sub>2</sub> D <sub>3</sub> Dexamethasone

4 days

2 days

8 - 10 days

Groups

OPG

OPG

— — —

— — —

100 ng/ml

— — —

— — —

100 ng/ml

100 ng/ml

100 ng/ml

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. 22A

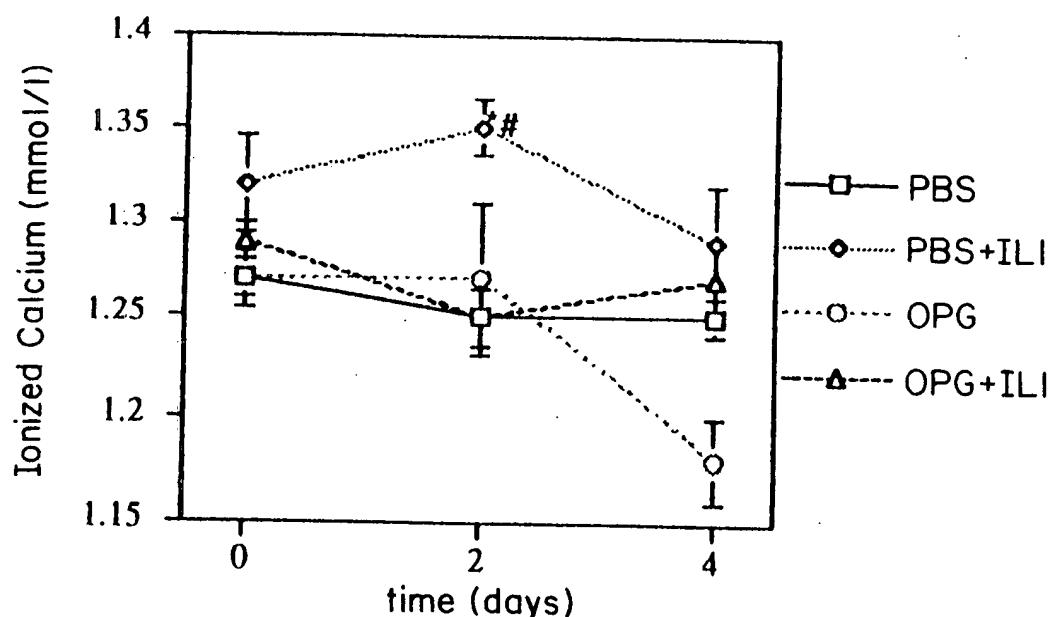
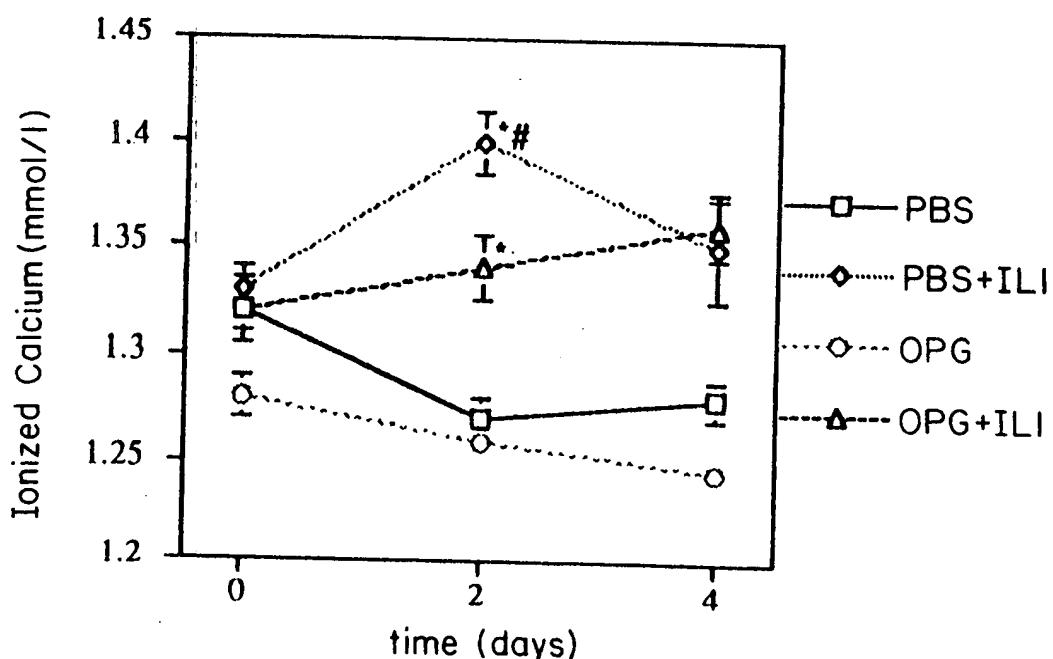


FIG. 22B



\* Different to PBS,  $p < 0.05$

# Different to OPG + IL1,  $p < 0.05$

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

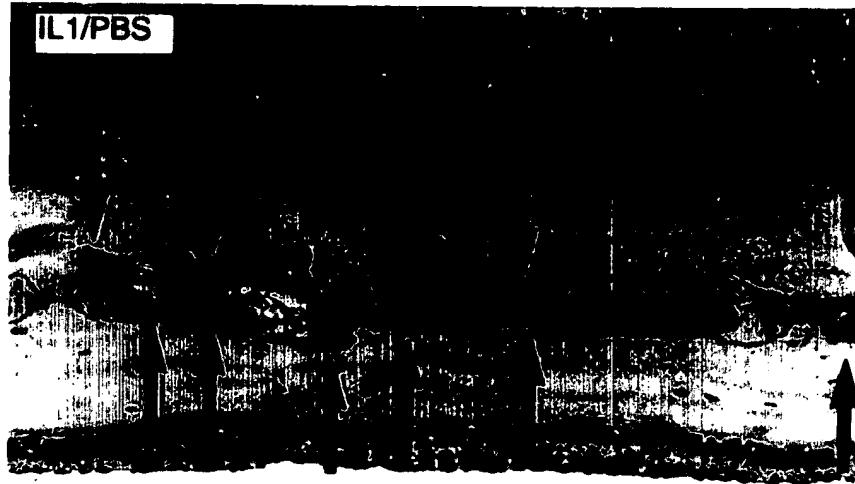
## FIG.23A

PBS/PBS



## FIG.23B

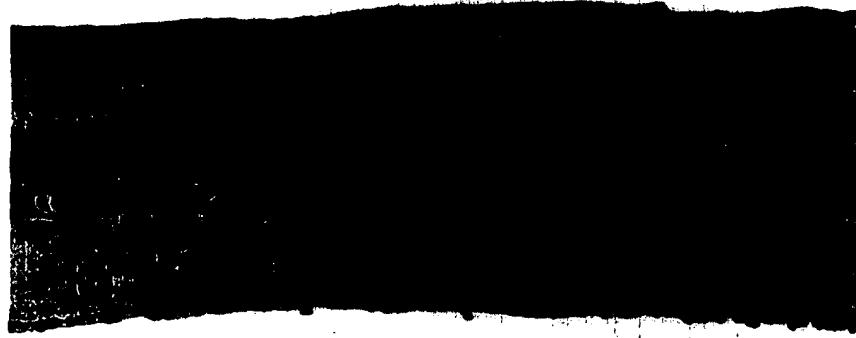
IL1/PBS



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG.23C

PBS/OPG



## FIG.23D



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.24B

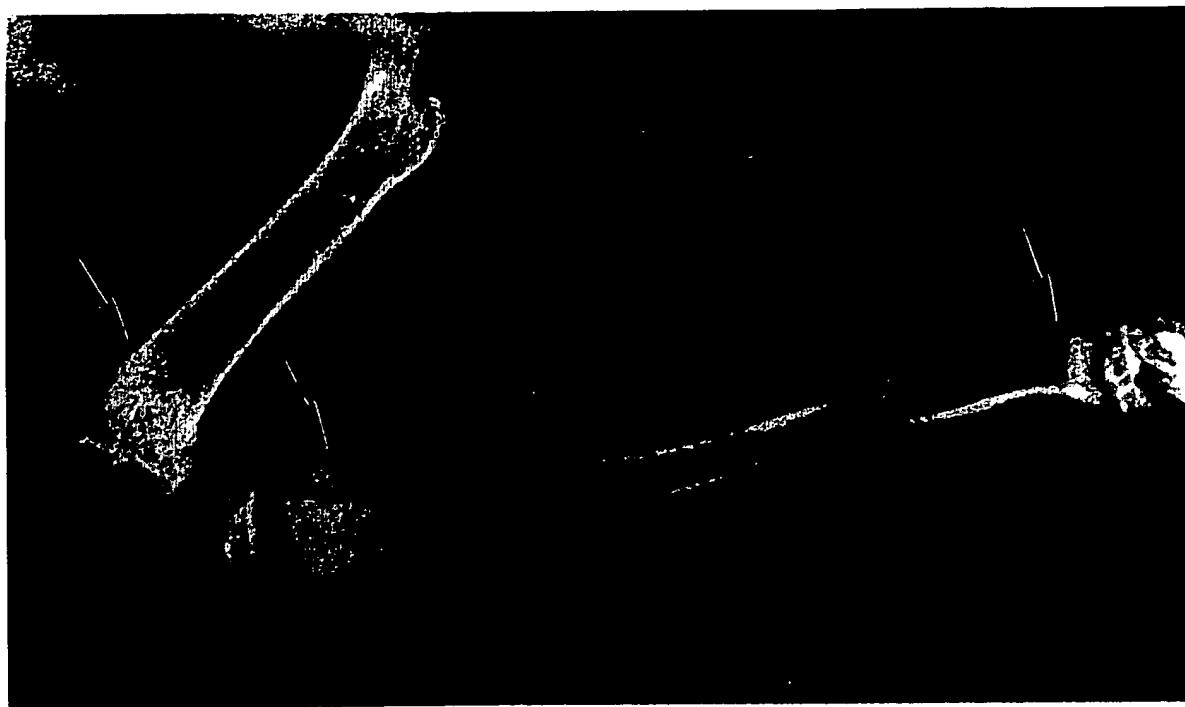
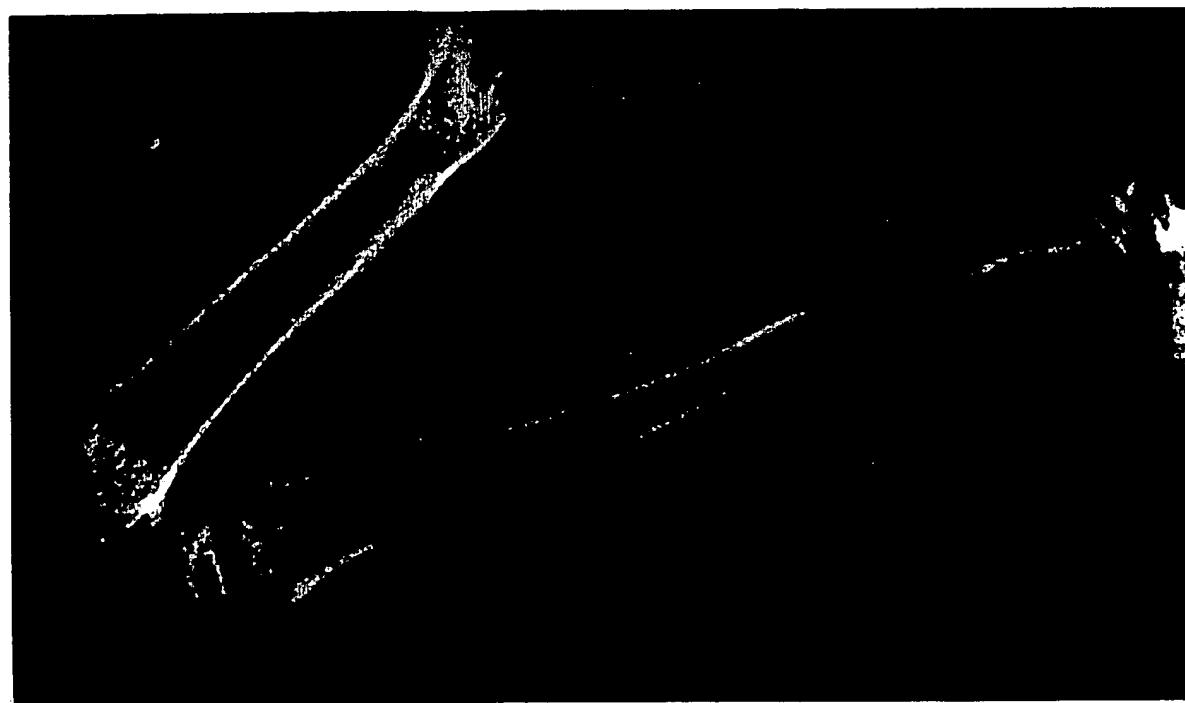
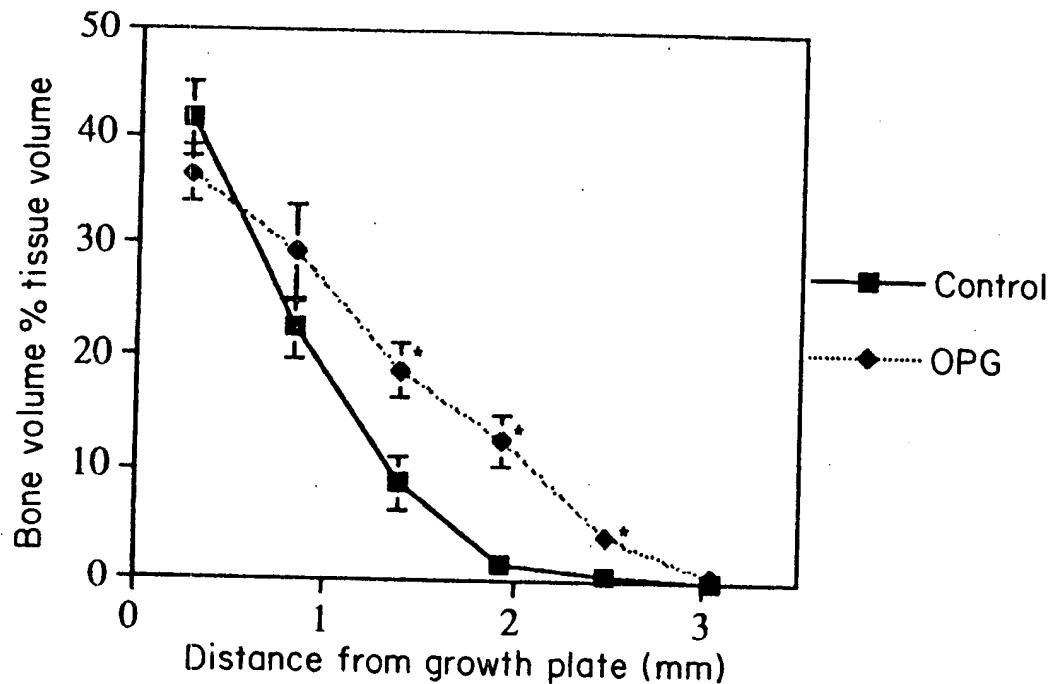


FIG.24A



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. 25



\* Different to control  $p < 0.01$

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

**FIG. 26A**

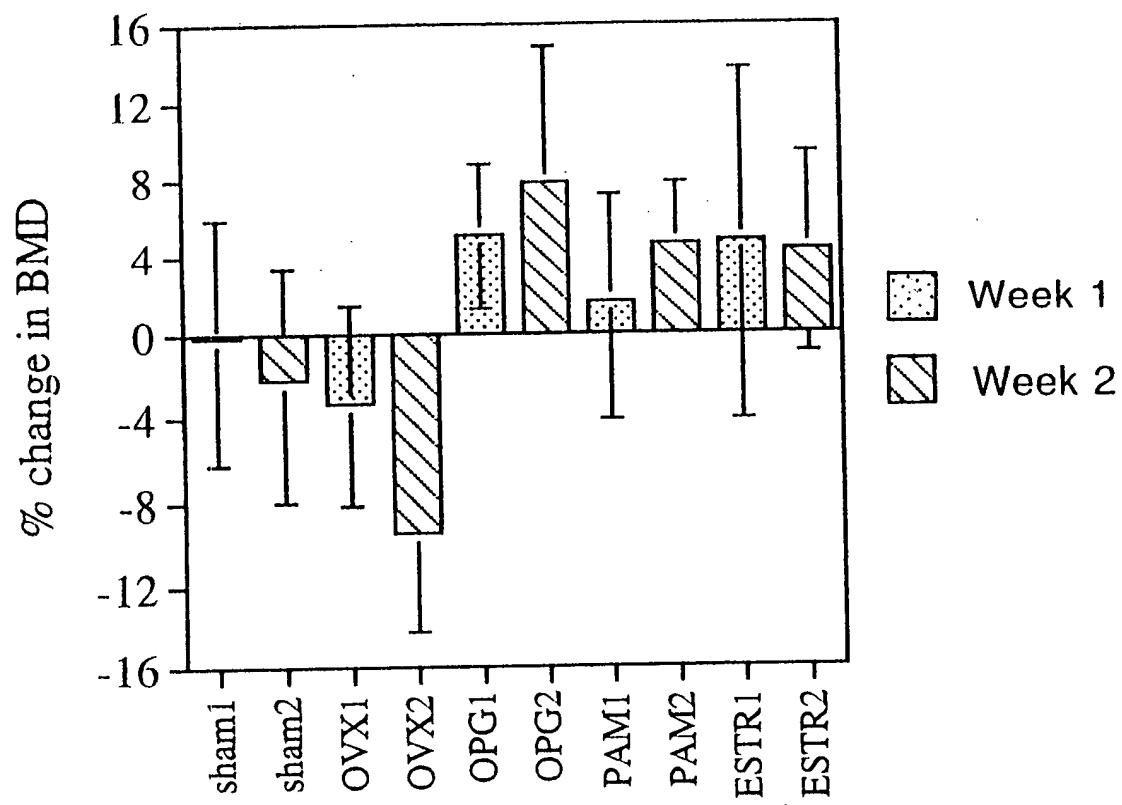


**FIG. 26B**



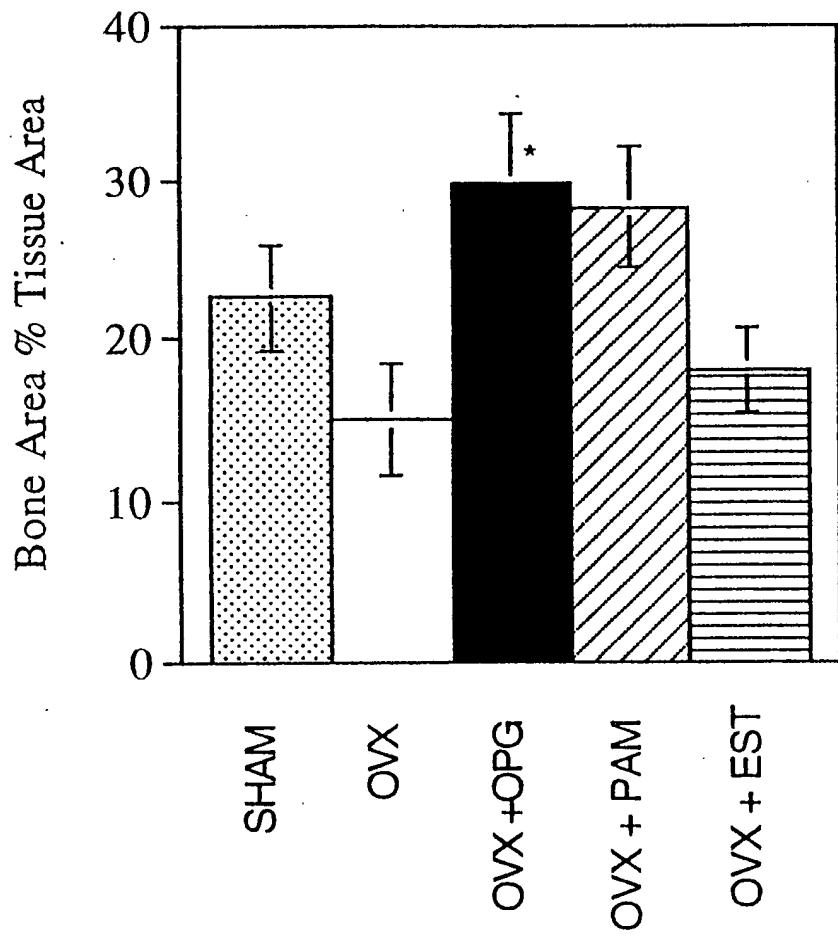
TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. 27



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. 28



\* Different to OVX  $p < 0.05$

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29A

### DraIII

CATGGAAATGTCAGAGTGGAGAACCAACCGAGTGCCACTGCAGCACTTGTATTATCA  
1 -----+-----+-----+-----+-----+-----+ 60  
GTACCCTTACAGTCTCACCTCTGGTGTGGCTACGGTACGTCGTGAACAATAATAGT  
  
CAAATCCTAATAGTTGCAGTGGCCTGCTGATGATGGCTGACTTGCTCAAAAGGAAA  
61 -----+-----+-----+-----+-----+-----+ 120  
GTTTAGGATTATCAAACGTACCCGGAACGACTACTACCGACTGAACGAGTTCCCTTT  
  
TTAATTTGTCCAGTGTCTATGGCTTGTGAGATAAAACCTCCTTCCCTGCCATACCA  
121 -----+-----+-----+-----+-----+-----+ 180  
AATTAAACAGGTACAGATAACCGAAACACTCTATTTGGGAGGAAAAGGAACGGTATGGT  
  
TTTTAACCTGCTTGAGAATATACTGCAGCTTATTGCTTCTCCTTACATAAATA  
181 -----+-----+-----+-----+-----+-----+ 240  
AAAAATTGGACGAAACTCTTATATGACGTCGAAATAACGAAAAGAGGAATAGGATGTTAT  
  
TAATCAGTAGTCTTGATCTTCATTGGAATGAAATATGGCATTAGCATGACCATAAA  
241 -----+-----+-----+-----+-----+-----+ 300  
ATTAGTCATCAGAACTAGAAAAGTAAACCTTACTTATACCGTAAATCGTACTGGTATT  
  
AAGCTGATTCCACTGGAAATAAAAGTCTTTAAATCATCACTCTATCACTGAATTCTAATT  
301 -----+-----+-----+-----+-----+-----+ 360  
TTCGACTAAGGTGACCTTATTCAAGAAAATTAGTAGTGAGATAGTGACTIONAAGATTAA  
  
TTTCTGAAAAGTTCAAGCCAGTTACTTTGATAGGATTAACGGAAGGGAGTGAGCCAG  
361 -----+-----+-----+-----+-----+-----+ 420  
AAAAGACTTTCAAAGTTCGGTCAATGAAAACCTATCCTAATTGCCTCCCTCACTCGGTC

### XcmI

TGGGTGAGGTGGGTTCCATGTAGTCATGGCTAATACTGGAGAACCTTATTCTAACCA  
421 -----+-----+-----+-----+-----+-----+ 480  
ACCCACTCCACCCAAAGGGTACATCAGTTACCGGATTATGACCTCTTAGAATAAGATTGGT  
  
AGCCTTCCAGAGCAAGCTGTGAGCCCCCTCAGACAGTGGCTACTCATGAGACAGTCCATT  
481 -----+-----+-----+-----+-----+-----+ 540  
TCGGAAGGTCTCGTCGACACTCGGGAGTCTGTCACCCGATGAGTACTCTGTCAGGTAA  
  
GGGGTAAAGGAAGAAAATATAACTCTATTCTATTGACATTGTCACATTGTCTTAGATGC  
541 -----+-----+-----+-----+-----+-----+ 600  
CCCCATTCTCTTTATATTGAAGATAAGATAAGTAAACGTGTAACAGAAATCTACG  
  
CCATTTGGGTGAGTTTATAGAAGTACAGCTACATTAAAAAATAGAACTGATAATAGATA  
601 -----+-----+-----+-----+-----+-----+-----+ 660  
GGTAAACCCACTCAAAATATCTCATGTCGATGTAATTCTTATCTGACTATTCTAT

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29B

AGGCTTTAAAAAAACTTCATTCAATCACCAAGTTGTCAAGATTCCATTCAAAGTGA  
661 -----+-----+-----+-----+-----+-----+-----+-----+ 720  
TCCGAAATTTTTGAAGTAAGTAGTGGTAAACAGTTCAAGGTAAAGTTCACTTTT  
  
CCAATTTCTAACGGGTTGGTAAACACACAGCAGATGGCAGGGTGAAAAATTAAAGTGAGTGC  
721 -----+-----+-----+-----+-----+-----+-----+-----+ 780  
GGTAAAGATTGCCAACCATTTGTGCGTCTACCGTCCACTTTAATTCACTCACG  
  
ATGTACCTTAAAGAAACACTGAAATGCACACACATTACTTAACCTGCTCATTCA  
781 -----+-----+-----+-----+-----+-----+-----+-----+ 840  
TACATGGAAATTCTTGTGACTTACGTGTGTAATGAATTGGACGAGTAAGTAAATA  
  
TTACATATAGTCTGGGTGTACAAAATTAGAAATAACATATGGGGCGGGGCCTA  
841 -----+-----+-----+-----+-----+-----+-----+-----+ 900  
AATGTATATCAGAACCCACATGTTAAATCTTATTTATGTATACCCCCGCCCGGAAT  
  
GCTGCACAAATAGGATGCGCGGCGGGCCTTGGTAGGGGCGGAGCCTAGCTGCACAAATA  
901 -----+-----+-----+-----+-----+-----+-----+-----+ 960  
CGACGTGTTATCCTACGCGCCGCCCGAACCATCCCCGCCTCGGAATCGACGTGTTAT  
  
GGATGCGCGGCGGGCCTTGGTGGGGCGGGCTAAGCTGCGCAAGTGGTACACAGCTCA  
961 -----+-----+-----+-----+-----+-----+-----+-----+ 1020  
CCTACGCGCCGCCCGAACCAACCCCCGCCCGATTGACGCGTTACCATGTGTCGAGT  
  
GGGCTGCGATTCGCGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTGGTAGGATTTA  
1021 -----+-----+-----+-----+-----+-----+-----+-----+ 1080  
CCCGACGCTAAAGCGCGTTGAAC TGCGTTAGGATCGACACTCCGACCACCTAAAAT  
  
TCCCCGCTGCCATCATGGTCGACCATTGAACTGCATCGCCGTGTCCAAAATATGG  
1081 -----+-----+-----+-----+-----+-----+-----+-----+ 1140  
AGGGGCGACGGTAGTACCAAGCTGGTAAC TTGACGTAGCAGCGGCACAGGGTTTATACC  
  
GGATTGGCAAGAACGGAGACCTACCCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCC  
1141 -----+-----+-----+-----+-----+-----+-----+-----+ 1200  
CCTAACCGTTCTTGCCTCTGGATGGGACCGGAGGCGAGTCCTGCTCAAGTTCATGAAGG  
  
AAAGAATGACCACAACCTCTCAGTGGAAAGGTAAACAGAACATCTGGTAGGATTATGGTAGGA  
1201 -----+-----+-----+-----+-----+-----+-----+-----+ 1260  
TTTCTTACTGGTGTGGAGAAGTCACCTTCATTGTCTTAGACCAACTAACCCATCCT  
  
AAACCTGGTTCTCCATTCTGAGAAGAACGACCTTAAAGGACAGAACATATAGTTC  
1261 -----+-----+-----+-----+-----+-----+-----+-----+ 1320  
TTTGGACCAAGAGGTAAAGGACTCTTCTTAGCTGGAAATTCTGTCTTAATTATACAG  
  
SacI                    BstXI  
|                      |  
TCAGTAGAGAACTCAAAGAACCAACGAGGAGCTCATTTCTGCCAAAGTTGGATG

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29C

AfI<sup>II</sup>

ATGCCTTAAGACTTATTGAACAAACCGAATTGGCAAGTAAAGTAGACATGGTTGGATAG  
1381 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1440  
TACGGAATTCTGAATAACTGTTGGCCTAACCGTTCAATTTCATCTGTACCAAACCTATC  
  
TCGGAGGCAGTTCTGTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAGACTCTTG  
1441 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1500  
AGCCTCCGTCAAGACAAAATGGCCTTCGGTACTTAGTTGGTCCGGTGGAGTCTGAGAAC  
  
TGACAAGGATCATGCAGGAATTGAAAGTGACACGTTTCCCAGAAATTGATTGGGA  
1501 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1560  
ACTGTTCCCTAGTACGTCTAAACTTCACTGTGCAAAAAGGGTCTTAACTAAACCCCT  
  
AATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGAGGTCCAGGAGGAAAAGGCA  
1561 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1620  
TTATATTTGAAGAGGGTCTTATGGGTCCGCAGGAGAGACTCCAGGTCTCCTTTCCGT  
  
TCAAGTATAAGTTGAAGTCTACGAGAAGAAAGACTAACAGGAAGATGCTTCAGTTCT  
1621 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1680  
AGTTCATATTCAAACCTCAGATGCTCTTCTGATTGCTCTACGAAAGTTCAAGA

BgI<sup>II</sup>

CTGCTCCCCCTCTAAAGCTATGCATTTTATAAGACCATGGACTTTGCTGGCTTCTAGA  
1681 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1740  
GACGAGGGGAGGATTCGATACTGAAAAATATTCTGGTACCTGAAAACGACCGAAATCT  
  
TCTGAAACACTGAAATTGTCGCTTCTCATCTTCAGTGAGATTCCAAAGGATAGTACAGT  
1741 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1800  
AGACTTTGTGACTTTAACAGACGAAGAGTAGAAGTCACTCTAAGGTTCTATCATGTCA  
  
GACAGAACAGAATAGGCACTCTACAAAAAAAGAAAGAAAAACTAAGTAATAGCAA  
1801 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1860  
CTGTCTGTTCTTATCCGTGAGAGATGTTTTCTTTGATTCTTACCGTT  
  
GCATAATAGCTACTGTTAAGAACTCAGAGATAATGAATTGAGAATGGATACTGCTTGAAA  
1861 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1920  
CGTATTATCGATGACAATTCTTGAGTCTCTATTACTTAACTCTTACCTATGACGAACCTT  
  
TGAAAATTAAATAAGTTAGAAACTAAACTTTATAAAAATAAAAATGAGCATTAAAAAA  
1921 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1980  
ACTTTTAAATTATTCAATCTTGATTGAAATATTTTATTTTACTCGTAATT  
  
NheI

AAAAAAAAAAAAAAAAACCCCCCCCCCCCCCTGCAGCCAAGCTAGCTTGGAAATC  
1981 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2040

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29D

### BspLU11I

AGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAA  
2041 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2100  
TCCCCTATTGCGTCCTTCTTGTACACTCGTTCCGGTCGTTCCGGTCCTGGCATT  
  
AAAGGCCGCCTTGCTGGCTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAA  
2101 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2160  
TTTCCGGCGAACGACCGCAAAAGGTATCCGAGGCGGGGACTGCTCGTAGTGT  
  
TCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAGATAACCAGGCCTTCC  
2161 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2220  
AGCTGCGAGTTCACTCCACCGCTTGGCTGCTGATATTCTATGGTCCGAAAGG  
  
CCCTGGAAGCTCCCTCGTGCCTCTCCTGTTCCGACCCCTGCCGCTTACCGGATACCTGTC  
2221 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2280  
GGGACCTTCGAGGGAGCACCGAGAGGACAAGGCTGGACGGGAATGGCCTATGGACAG  
  
CGCCTTCTCCCTCGGGAAAGCGTGGCGTTCTCATAGCTCACGCTGTAGGTATCTCAG  
2281 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2340  
GCGGAAAGAGGGAAAGCCCTTCGCACCGCGAAAGAGTATCGAGTGCACATCCATAGAGTC  
  
TTCGGTGTAGGTCGTTCGCTCCAAGCTGGCTGTGCACGAACCCCCGTTAGCCGA  
2341 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2400  
AAGCCACATCCAGCAAGCGAGGTTCGACCCGACACACGTGCTGGGGCAAGTCGGGCT  
  
CCGCTGCGCCTTATCCGTAACATCGTCTTGAGTCCAACCCGTAAGACACCGACTTATC  
2401 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2460  
GGCGACGCGGAATAGGCCATTGATAGCAGAACTCAGGTTGGCCATTCTGTGCTGAATAG  
  
GCCACTGGCAGCAGCCACTGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTAC  
2461 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2520  
CGGTGACCGTCGTCGGTGACCAATTGCTCTCGCTCCATACATCCGCCACGATG  
  
AGAGTTCTGAAGTGGTGGCTTAACACTACGGCTACACTAGAAGGACAGTATTGGTATCTG  
2521 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2580  
TCTCAAGAACTTCACCAACCGGATTGATGCCATGTGATCTCCTGTCAATAACCATAGAC  
  
CGCTCTGCTGAAGCCAGTTACCTCGAAAAAGAGTTGGTAGCTCTGATCCGGCAAACA  
2581 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2640  
GCGAGACGACTTCGGTCAATGGAAGCCTTTCTCAACCATCGAGAACTAGGCCGTTGT

### HgiEII

AACCACCGCTGGTAGCGGTGTTTTGTTGCAAGCAGCAGATTACGCGCAGAAAAAA  
2641 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2700  
TTGGTGGCGACCATGCCACCAAAAAACAAACGTTCGTCGTCTAATGCGCGTCTTTTT  
  
AGGATCTCAAGAAGATCCTTGATCTTCTACGGGTCTGACGCTCAGTGGAACGAAAA  
2701 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2760

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## FIG. 29E

CTCACGTTAAGGGATTTGGTCATGAGATTATCAAAAGGATCTCACCTAGATCCTTT  
2761 -----+-----+-----+-----+-----+-----+-----+-----+ 2820  
GAGTGCAATTCCCTAAAACCACTACTCTAATAGTTTCCAGAAGTGGATCTAGGAAAA

AAATTAAAAATGAAGTTTAAATCAATCTAAAGTATATATGAGTAAACTGGTCTGACAG  
2821 -----+-----+-----+-----+-----+-----+-----+-----+ 2880  
TTAATTTTACTTCAAAATTAGTTAGATTCATATATACTCATTTGAACCAGACTGTC

TTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTCGTTCATCCAT  
2881 -----+-----+-----+-----+-----+-----+-----+-----+ 2940  
AATGGTTACGAATTAGTCACTCCGTGGATAGAGTCGCTAGACAGATAAAGCAAGTAGGTA

AGTTGCCTGACTCCCCGTGCTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCC  
2941 -----+-----+-----+-----+-----+-----+-----+-----+ 3000  
TCAACGGACTGAGGGCAGCACATCTATTGATGCTATGCCCTCCGAATGGTAGACCGGG

CAGTGCTGCAATGATAACCGCGAGACCCACGCTCACCGCTCCAGATTATCAGCAATAAA  
3001 -----+-----+-----+-----+-----+-----+-----+-----+ 3060  
GTCACGACGTTACTATGGCGCTCTGGGTGCGAGTGGCCGAGGTCTAAATAGTCGTTATT

CCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGCTGTCAACTTATCCGCCTCCATCCA  
3061 -----+-----+-----+-----+-----+-----+-----+-----+ 3120  
GGTCGGTCGGCCTTCCCGCTCGCGTCTCACCAGGACGTGAAATAGCGGAGGTAGGT

GTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTGCCAGTTAATAGTTGCGCAA  
3121 -----+-----+-----+-----+-----+-----+-----+-----+ 3180  
CAGATAATTAACAACGGCCCTCGATCTCATTCAAGCGGTCAATTATCAAACCGCGTT

CGTTGTTGCCATTGCTGCAGGCATCGTGGTGTACGCTCGTCTGGTATGGCTTCATT  
3181 -----+-----+-----+-----+-----+-----+-----+-----+ 3240  
GCAACAACGGTAACGACGTCCGTAGCACCACAGTGCAGCAGCAAACCATACCGAAGTAA

CAGCTCCGGTTCCCAACGATCAAGGCAGTTACATGATCCCCATGTTGTGAAAAAAGC  
3241 -----+-----+-----+-----+-----+-----+-----+-----+ 3300  
GTCGAGGCCAAGGGTTGCTAGTTCCGCTCAATGTTAGGGGTACAACACGTTTTTCG

EaeI  
PvuI GdiII

| |  
GGTTAGCTCCTCGGTCTCCGATCGTGTCAAGAAGTAAGTTGGCCGAGTGTATCACT  
3301 -----+-----+-----+-----+-----+-----+-----+-----+ 3360  
CCAATCGAGGAAGCCAGGAGGCTAGCAACAGTCTCATTCAACCGCGTCACAATAGTGA

CATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTC  
3361 -----+-----+-----+-----+-----+-----+-----+-----+ 3420  
GTACCAATACCGTCGTGACGTATTAAGAGAATGACAGTACGGTAGGCATTCTACGAAAAG

BcgI  
|  
TGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTG

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## FIG. 29F

CTCTTGCCCGGCGTCAACACGGATAATACCGGCCACATAGCAGAACTTTAAAAGTGCT  
3481 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3540  
GAGAACGGGCCGCAGTTGTGCCCTATTATGGCGCGGTGTACGTCTTCAAATTTCACGA

CATCATTGGAAAACGTTCTTCGGGGCGAAAACCTCTCAAGGATCTTACCGCTGTTGAGATC  
3541 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3600  
GTAGTAACCTTTGCAAGAAGCCCCGCTTGAGAGTTCTAGAATGGCGACAACCTAG

CAGTTCGATGTAACCCACTCGTGCACCCAACGTGATCTTCAGCATCTTTACTTCAACCAG  
3601 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3660  
GTCAAGCTACATTGGGTGAGCACGTGGTTGACTAGAAGTCGTAGAAAATGAAAGTGGTC

CGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGAAAAAGGGAATAAGGGCGAC  
3661 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3720  
GCAGAACCCACTCGTTTGTCTTCGTTTACGGCTTTTCCCTTATTCCGCTG

SspI  
|  
ACGGAAATGTTGAATACTCATACTCTTCCTTTCAATATTATTGAAGCATTATCAGGG  
3721 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3780  
TGCCTTACAACTTATGAGTATGAGAAGGAAAAGTTATAAACTTCGTAAATAGTCCC

TTATTGTCTCATGAGCGGATACATATTGAATGTATTAGAAAATAACAAATAGGGGT  
3781 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3840  
AATAACAGAGTACTCGCTATGTATAAACTACATAATCTTTATTGTTATCCCCA

TCCGCGCACATTCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATGAC  
3841 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3900  
AGGCGCGTGTAAAGGGCTTTCACGGTGGACTGCAGATTCTTGGTAATAATAGTACTG

ATTAACCTATAAAAATAGGCGTATCACGAGGCCCTTCGTCTTCAAGAATTCCCTGTGGA  
3901 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3960  
TAATTGGATATTTTATCCGCATAGTGCCTCCGGAAAGCAGAAGTCTTAAGGGACACCT

ATGTGTGTCAAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAA  
3961 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 4020  
TACACACAGTCAATCCCACACCTTCAGGGTCCGAGGGTCCGTCCGTCTTCATACGTT

GCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCA  
4021 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 4080  
CGTACGTAGAGTTAATCAGTCGTTGGTCCACACCTTCAGGGTCCGAGGGTCCGTCCGT

GAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGTCCGCCCTAACTCCGC  
4081 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 4140  
CTTCATACGTTCGTACGTAGAGTTAATCAGTCGTTGGTATCAGGGGGGATTGAGGCG

CCATCCCCCCCCCTAATCCGCCAGTCCGCCATTCTCCGCCCATGGCTGACTAATT  
4141 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 4200

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## FIG. 29G

### SfiI

TTTTATTTATGCAGAGGCCGAGGCCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAG  
4201 -----+-----+-----+-----+-----+-----+-----+-----+ 4260  
AAAAATAAAATACGTCTCCGGCTCCGGGGAGCCGGAGACTCGATAAGGTCTTCATCACTC

### AvrII

GAGGCTTTTGAGGCCTAGGCTTTGCAAAAAGCTGGTCAGGCTCGCATCTCTCCTT  
4261 -----+-----+-----+-----+-----+-----+-----+ 4320  
CTCCGAAAAAACCTCCGGATCCGAAAACGTTTCGACCAGCTCCGAGCGTAGAGAGGAA  
  
CACGCGCCCGCCGCCTACCTGAGGCCATCCACGCCGTTGAGTCGCCTCTGCCGC  
4321 -----+-----+-----+-----+-----+-----+-----+ 4380  
GTGCGCGGGCGGCGGGATGGACTCCGGCGGTAGGTGCGGCCACTCAGCGCAAGACGGCG  
  
CTCCCGCTGTGGTGCCTCCTGAAC TGCGTCCGCCGTCTAGGTAAGTTAAAGCTCAGGT  
4381 -----+-----+-----+-----+-----+-----+-----+ 4440  
GAGGGCGGACACCACGGAGGACTTGACGCAGGCCAGATCCATTCAAATTGAGTCCA

### NgoAIV

CGAGACCGGGCCTTGTCCGGCGCTCCCTGGAGCCTACCTAGACTCAGCCGGCTCTCCA  
4441 -----+-----+-----+-----+-----+-----+-----+ 4500  
GCTCTGGCCCGGAAACAGGCCGCGAGGGAACCTCGGATGGATCTGAGTCGGCGAGAGGT  
  
CGCTTGCCCTGACCTGCTCAACTCTACGTCTTGTCTGTTCTGCGCC  
4501 -----+-----+-----+-----+-----+-----+-----+ 4560  
GCGAACCGGACTGGGACGAACGAGTTGAGATGCAGAAACAAAGCAAAAGACAAGACGGG

### HpaI

GTTACAGATCCGTCAGGAACTGAAAAACCAGAAAGTTAACTGGTAAGTTAGTCTTTT  
4561 -----+-----+-----+-----+-----+-----+-----+ 4620  
CAATGTCTAGGCAGCTCCTTGACTTTGGTCTTCATTGACCATTCAAATCAGAAAAA

### Psp5II BamHI

GTCTTTATTCAGGTCCGGATCCGGTGGTGGTGCAGAACATCAAAGAACTGCTCCTCAGTG  
4621 -----+-----+-----+-----+-----+-----+-----+ 4680  
CAGAAAATAAGTCCAGGGCTAGGCCACCACGTTAGTTCTTGACGAGGAGTCAC  
  
GATGTTGCCCTTACTCTAGGCCTGTACGGAAGTGTACTTCTGCTCTAAAGCTGCTGC  
4681 -----+-----+-----+-----+-----+-----+-----+ 4740  
CTACAACGGAAATGAAGATCCGGACATGCCTTCACAATGAAGACGAGATTTGACGACG

### HindIII XbaI

### BssHII

AACAAGCTCTAGACCACCATGAACAAGTTGCTGTGCTGCGCGCTCGTGTGACAT  
4741 -----+-----+-----+-----+-----+-----+-----+ 4800  
TTGTTCGAAGATCTGGTGGTACTTGTCAACGACACGACGCGCAGCAGACACCTGTA

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## FIG. 29H

CTCCATTAAGTGGACCACCCAGGAAACGTTCTCAAAGTACCTTCATTATGACGAAGA  
4801 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4860  
GAGGTAAATTCACTGGTGGGCTTGCAAAGGAGGTTCATGGAAGTAATACTGCTTCT  
b S I K W T T Q E T F P P K Y L H Y D E E -

KpnI

AACCTCTCATCAGCTGTTGACAAATGTCCTCCTGGTACCTACCTAAAACAACACTG  
4861 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4920  
TTGGAGAGTAGTCGACAACACACTGTTACAGGAGGACATGGATGGATTTGTTGTGAC  
b T S H Q L L C D K C P P G T Y L K Q H C -

TACAGCAAAGTGGAAAGACCGTGTGCGCCCCCTGCCCTGACCACTACTACACAGACAGCTG  
4921 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4980  
ATGTCGTTTCACCTCTGGCACACGCGGGGAACGGGACTGGTATGATGTGTCTGTCGAC  
b T A K W K T V C A P C P D H Y Y T D S W -

GCACACCAGTGACGAGTGTCTATACTGCAGCCCCGTGTGCAAGGAGCTGCAGTACGTCAA  
4981 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5040  
CGTGTGGTCACTGCTCACAGATATGACGTCGGGCACACGTTCTCGACGTATGCAGTT  
b H T S D E C L Y C S P V C K E L Q Y V K -

RleAI BsmI

GCAGGAGTGCAATCGCACCCACAACCGCGTGTGCGAATGCAAGGAAGGGCGTACCTTGA  
5041 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5100  
CGTCCTCACGTTAGCGTGGGTGTTGGCGCACACGCTTACGTTCTCCCGCGATGGAAC  
b Q E C N R T H N R V C E C K E G R Y L E -

GATAGAGTTCTGCTTGAACATAGGAGCTGCCCTCTGGATTTGGAGTGGTGCAGCTGG  
5101 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5160  
CTATCTCAAGACGAACTTGTATCCTCGACGGGAGGACCTAACCTCACCACGTTCGACC  
b I E F C L K H R S C P P G F G V V Q A G -

BsmBI

AACCCCAGAGCGAAATACAGTTGCAAAGATGTCCAGATGGGTTCTCTCAAATGAGAC  
5161 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5220  
TTGGGGTCTCGCTTATGTCAAACGTTCTACAGGTCTACCCAAGAAGAGTTACTCTG  
b T P E R N T V C K R C P D G F F S N E T -

GTCATCTAAAGCACCTGTAGAAAACACACAAATTGCAGTGTCTTGGTCTCTGCTAAC  
5221 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5280  
CACTAGATTTCTGGACATCTTGTGTTAACGTACAGAAACCAGAGGAGCATTG  
b S S K A P C R K H T N C S V F G L L L T -

BspEI

TCAGAAAGGAAATGCAACACACGACAACATATGTTCCGGAAACAGTGAATCAACTAAAA  
5281 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5340

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## **FIG. 29 I**

**Sall**                    **BmgI**  
|                        |  
AGTCGACAAACTCACACATGCCACCGTGCCCAGCACCTGAACCTCCTGGGGGGACCGTC  
5341 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5400  
TCAGCTGTTTGAGTGTACGGTGGCACGGTCGTGGACTTGAGGACCCCCCTGGCAG  
b      V D K T H T C P P C P A P E L L G G P S -  
  
AGTCTTCCTCTTCCCCCAAAACCAAGGACACCCCATGATCTCCGGACCCCTGAGGT  
5401 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5460  
TCAGAAGGAGAAGGGGGTTTGGGTCCTGTGGAGTACTAGAGGGCCTGGGACTCCA  
b      V F L F P P K P K D T L M I S R T P E V -  
  
**BtrI**  
|  
CACATGCGTGGTGGACGTGAGCCACGAAGACCCGTAGGTCAAGTTCAACTGGTACGT  
5461 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5520  
GTGTACGCACCACCTGCACTCGGTGCTTCTGGACTCCAGTTCAAGTTGACCATGCA  
b      T C V V V D V S H E D P E V K F N W Y V -  
  
**SacII**  
|  
GGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCAC  
5521 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5580  
CCTGCCGCACCTCCACGTATTACGGTCTGTTCGGCGCCCTCCTCGTCATGTTGTCGTG  
b      D G V E V H N A K T K P R E E Q Y N S T -  
  
GTACCGTGTGGTCAGCGTCCTCACCGTCTGCACCAAGGACTGGCTGAATGGCAAGGAGTA  
5581 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5640  
CATGGCACACCAGTCGCAAGGAGTGGCAGGACGTGGCCTGACCGACTTACCGTTCCAT  
b      Y R V V S V L T V L H Q D W L N G K E Y -  
  
CAAGTGCAAGGTCTCCAACAAAGCCCTCCAGCCCCCATCGAGAAAACCATCTCAAAGC  
5641 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5700  
GTTCACGTTCCAGAGGTTGTTGGGAGGGTAGCTTTGGTAGAGGTTTCG  
b      K C K V S N K A L P A P I E K T I S K A -  
  
**SmaI**  
|  
CAAAGGGCAGCCCCGAGAACCAACAGGTGTACACCCATGCCGGATGAGCTGAC  
5701 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5760  
GTTTCCCGTCGGGCTCTGGTGTCCACATGTGGGACGGGGTAGGGCCCTACTCGACTG  
b      K G Q P R E P Q V Y T L P P S R D E L T -  
  
CAAGAACCAAGGTCAACCTGCCCTGGTCAAAGGCTTCTATCCCAGCGACATGCCGT  
5761 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5820  
GTTCTTGGTCCAGTCGGACTGGACGGACCAAGTTCCGAAGATAGGGTCGCTGTAGCGGCA  
b      K N Q V S L T C L V K G F Y P S D I A V -  
  
GGAGTGGGAGAGCAATGGCAGCCGGAGAACAACTACAAGACCAACGCCCTCCGTGCTGGA  
5821 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 5880

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## FIG. 29J

### AarI

CTCCGACGGCTCCTTCTTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCA  
5881 -----+-----+-----+-----+-----+-----+-----+-----+ 5940  
GAGGCTGCCGAGGAAGAAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGT  
b S D G S F F L Y S K L T V D K S R W Q Q -

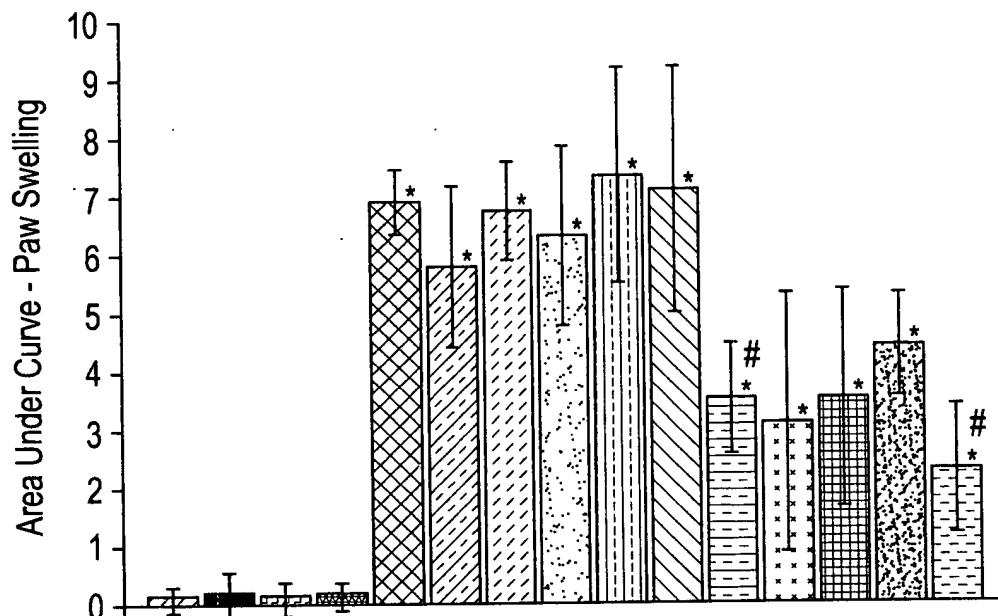
### SapI

GGGGAACGTCTTCTCATGCTCCGTATGCATGAGGCTCTGCACAACCACTACACGCAGAA  
5941 -----+-----+-----+-----+-----+-----+-----+-----+ 6000  
CCCCCTGCAGAACAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTATGTGCGTCTT  
b G N V F S C S V M H E A L H N H Y T Q K -

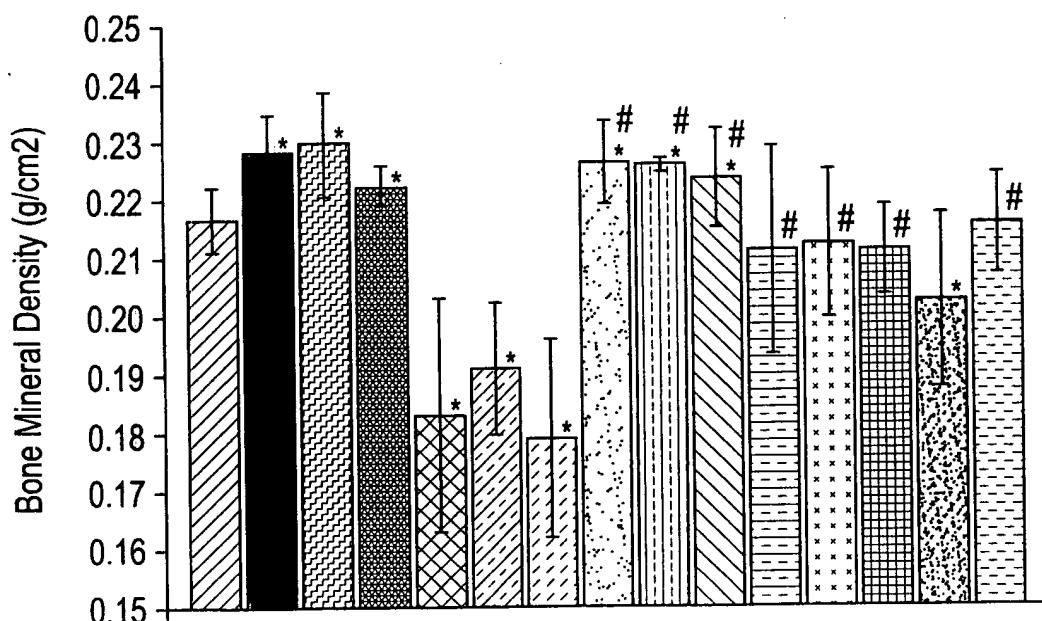
GAGCCTCTCCCTGTCTCCGGTAAATGATAACTCGAC  
6001 -----+-----+-----+-----+-----+ 6037  
CTCGGAGAGGGACAGAGGCCATTACTATTGAGCTG  
b S L S L S P G K \* \*

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**FIG. 30A-1**



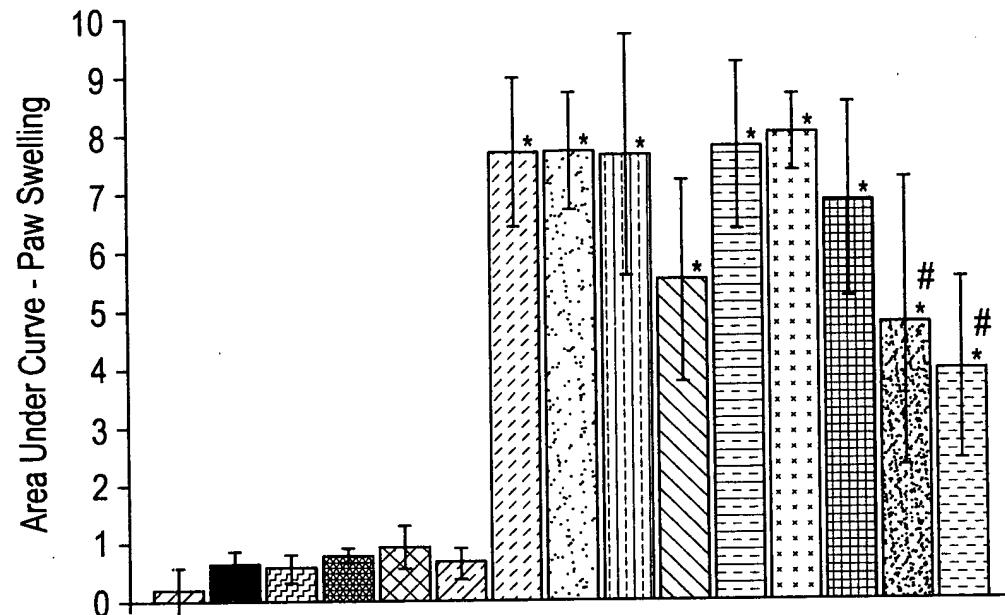
**FIG. 30A-2**



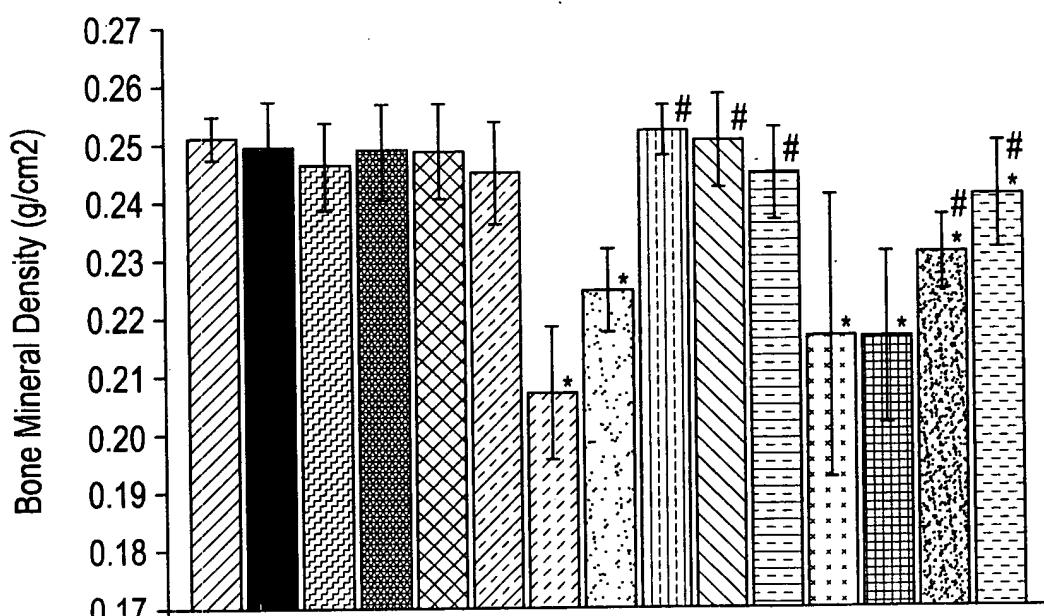
- ▨ Normal (NT)
- █ Normal + 4 mg/kg OPG-Fc (s.c.)
- ▨ Normal + 1.0 mg/kg OPG-Fc (s.c.)
- ▨ Normal + 0.25 mg/kg OPG-Fc (s.c.)
- ▨ AdA Control
- ▨ AdA + CSEP (2ML1)
- ▨ AdA + 0.025 mg/kg Dexamethasone (s.c.)
- ▨ AdA + 0.05 mg/kg Dexamethasone (s.c.)
- ▨ AdA + 0.1 mg/kg Dexamethasone (s.c.)
- ▨ AdA + 0.2 mg/kg Dexamethasone (s.c.)
- ▨ AdA + 0.5 mg/kg Dexamethasone (s.c.)

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**FIG. 30B-1**



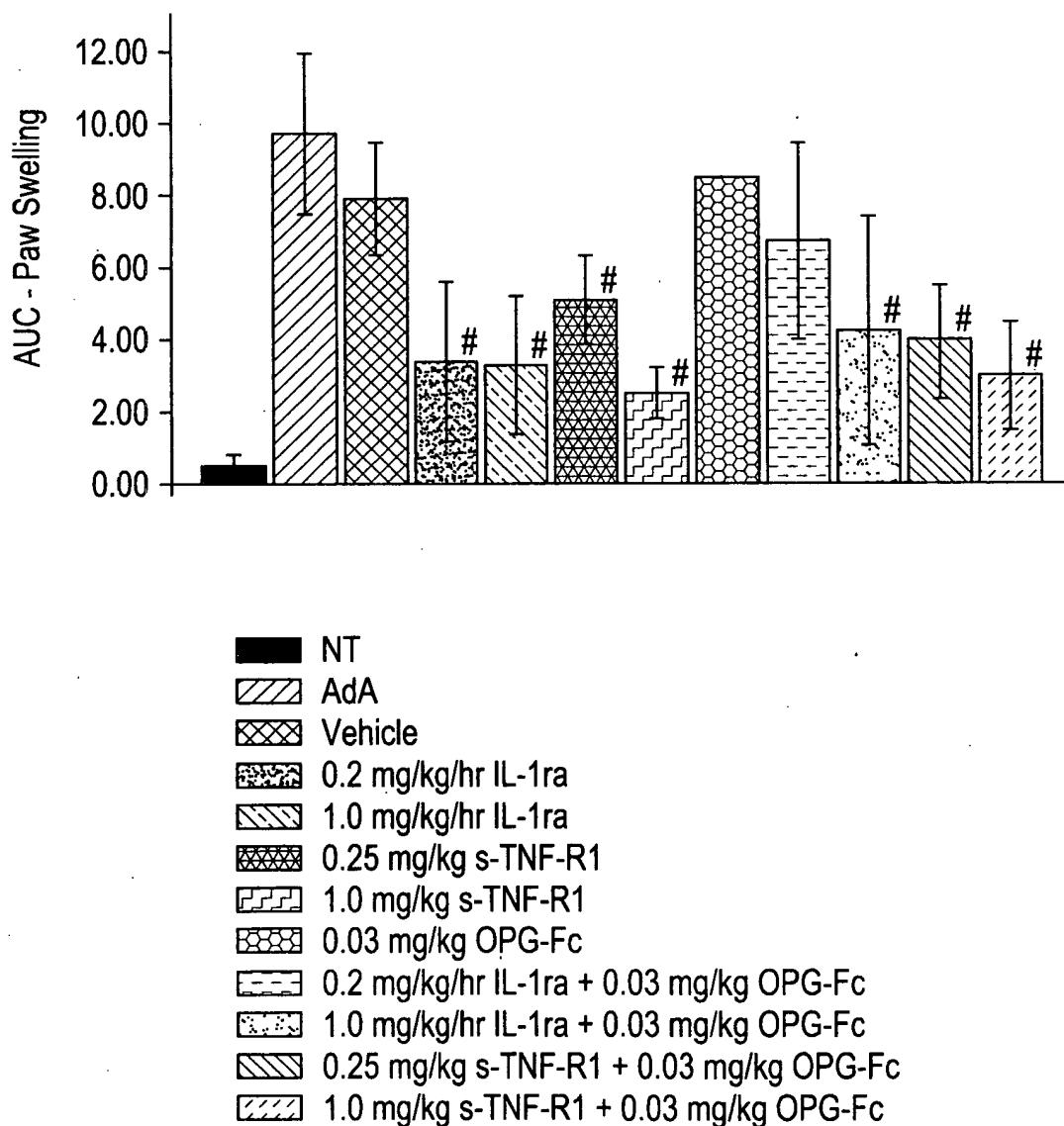
**FIG. 30B-2**



- ▨ Normal
- █ Normal + 1.0 mg/kg OPG-Fc (s.c.)
- ▨ Normal + 0.25 mg/kg OPG-Fc (s.c.)
- ▨ Normal + 0.0625 mg/kg OPG-Fc (s.c.)
- ▨ Normal + 0.016 mg/kg OPG-Fc (s.c.)
- ▨ Normal + 0.004 mg/kg OPG-Fc (s.c.)
- ▨ AdA control
- ▨ AdA + 1.0 mg/kg OPG-Fc (s.c.)
- ▨ AdA + 0.25 mg/kg OPG-Fc (s.c.)
- ▨ AdA + 0.0625 mg/kg OPG-Fc (s.c.)
- ▨ AdA + 0.016 mg/kg OPG-Fc (s.c.)
- ▨ AdA + 0.004 mg/kg OPG-Fc (s.c.)
- ▨ AdA + 5.0 mg/kg/hr IL-1ra (2ML1)
- ▨ AdA + 0.07 mg/kg Dexamethasone (s.c.)

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FIG. 31A



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FIG. 31B

